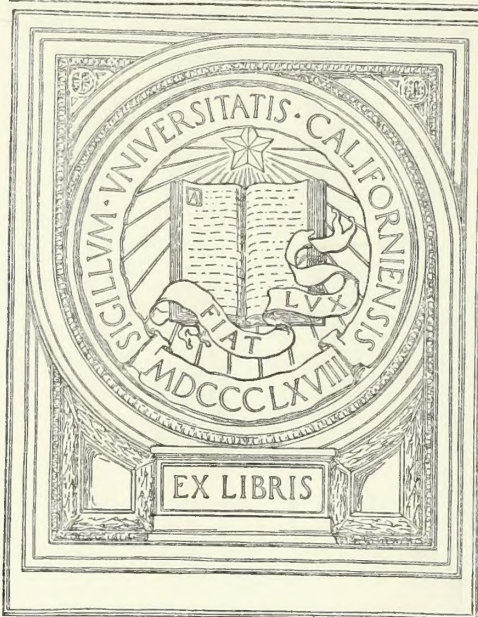






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### THE DETERMINATION OF SERUM AND URINE SALICYL LEVELS DURING TREATMENT WITH SALICYL DRUGS

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The initial purpose of this study was an attempt to improve the method of Coburn-Brodie<sup>1, 2</sup> for the determination of salicyl radicals in the blood. In an article about the treatment of rheumatic fever<sup>4</sup> with high detoxified doses of salicylates, I pointed out that it is of great importance to check the blood and urine salicyl levels during treatment. Without such a control it happens too often that the prescribed doses are not taken by the patients. Repeatedly I heard that the treatment with high doses of salicylates was declared ineffective, whereas a simple check of the blood and urine salicyl levels would have discovered fraud or negligence or bad absorption of salicyl compounds, given in tablets. These causes of low salicyl levels in the blood can easily be distinguished from temporary hypersecretion of the drug by the kidney which lowers, of course, also the serum salicyl levels.

My experience with the Coburn-Brodie method was that the results were often lower than was expected. This fact was also observed by the late pediatrician Chester Stewart. In an attempt to discover the cause of these observations, I tried several modifications of the Coburn-Brodie method. I replaced the ethylen-dichloride extraction

which is part of that method, by protein-precipitation, using the blood filtrate. During these investigations which were done shortly after the publication of Coburn's article in 1943, that is four years ago, I made an interesting observation which led to the development of a new, much simpler method which is now regularly used in laboratories of Charity Hospital, New Orleans. Accidentally a drop of a solution of ferric nitrate fell into the clear serum of a patient who was treated with large doses of salicylates. The serum showed a strong brown-violet color. I decided to examine the possibility of replacing the extraction procedure and the deproteinization procedure by a method, based upon this accidental finding. I examined first a large number (about sixty) of sera of patients who had had no drugs during 48 hours. Never a trace of a color-reaction was seen with the ferric nitrate solution. On the other hand, if the patient had taken small amounts of salicyl compounds, one hour before the drawing of the blood, the color-reaction appeared with ferric nitrate, but not yet with the extraction-method. Therefore the here described method is more sensitive.

#### PRINCIPLE OF THE HERE DESCRIBED METHOD

To 0.5 c.c. of clear non-hemolytic serum is added an iron-nitric acid reagent. If the serum contains more than 4 mg. per cent salicyl radicals, a color appears which is brownish in the lower and violet in the higher concentrations. In spite of these two colors, the optical density in a photoelectric colorimeter, produced by increasing salicyl concentrations, increases in a straight line. The cause of this unexpected fact is appar-

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ently that all the colors are mixtures of brown and violet.

Accurate determinations are made with a photoelectric colorimeter, (abbreviated PEC). A standard curve, prepared with standard solutions of sodium salicylate, has to be made for every PEC, because with three PEC of the same make, I found differences up to 20 divisions with the same colored serum. The preparation of the standard solutions and the calculation will be described in a more extensive article which will be published in one of the next numbers of the *Acta Medica Scandinavica*. Approximative estimations can be made with the aid of a color-chart which will soon be available in stores of laboratory supplies.

#### REAGENT

Only one reagent is necessary. After many trials the following mixture was chosen. Weigh out five grams of ferric nitrate. Dissolve this in 98 c.c. of aqua dest. Add 2 c.c. of concentrated nitric acid. (The sequence of additions is of importance). This reagent will be called: "Iron Reagent" or I. R.

#### PREPARATION FOR THE UNKNOWN SERUM

For making the mixture the following sequence is necessary:

Iron reagent	0.3 c.c.
Aquae dest.	7.2 c.c.
Serum	0.5 c.c.

(clear, non-hemolytic)

No filtration is necessary, if clear serum is used. If the serum is cloudy by some mistake (*vide infra*), then it is better to repeat the drawing of the blood, but approximative results can be obtained by filtration of the mixture through filters which remove very small particles, for example, Whatman filter No. 5 or S & S 602. Hemolytic serum should never be used. In the beginning of this investigation, I received several samples of cloudy or hemolysed serum. I could eliminate these mistakes by sterilizing the syringe and needle in hot air or in an autoclave but not by boiling, and by heating the tubes previously in order to remove the moisture on the inside.

Serum gives more reliable results than plasma, because I saw that different

amounts of anticoagulants, present in the plasma, may influence the color formation. Allow five minutes for the development of the color and read within the next few hours. The blood should be *always* drawn *just one hour after the latest dose of the drug*, in order to be able to compare the results with determinations on other days. At this time the "serum-salicyl" is about at its highest point.

In using the color chart, mentioned above, the tube is placed at an angle of 45° in a special rack which allows the light to fall just behind the colored fluid. (This special rack with a color-chart will be available as laboratory supply). If a PEC is present in the laboratory and a standard salicyl curve is made, it takes, of course, only little more time to obtain very accurate results.

In the more extensive article (*vide supra*) a table of observations will be published, showing a comparison between the results here described method and the Coburn-Brodie method. The results of the Coburn-Brodie method were 7 to 18 per cent lower than those with the here described method. Such large differences in the results explain the inconsistency which was also observed by the late Dr. Stewart, as mentioned above. Another table in that article shows that the results with the here described method are about the same in cases treated with or without the addition of sodium bicarbonate. This contradicts the publication of Smull et al.<sup>3</sup> which was the impulse of a nation-wide epidemic of intravenous injections of salicylates, without bicarbonate, in order to reach higher blood salicyl levels. Several patients died from this treatment. Also the observations of Huntington et al.<sup>5</sup> show that the results of Smull et al. are erroneous.

#### DETERMINATION OF THE URINE-SALICYL LEVEL

In this article only the principle of this determination can be mentioned. For details I refer to the extensive article, mentioned above. The principle is just the same as it is for serum salicyl determinations. The 0.5 c.c. serum is only replaced by 0.05 c.c.



of urine and as result is reported the quantity "urine-salicyl" excreted in the two-hour period, following the administration of the drug. This is necessary in order to eliminate the influence of the diuresis. Routine examinations of "urine-salicyl" are not yet described in the literature, as far as I could ascertain. This simple determination may replace a large part of the serum salicyl determinations, in a similar manner as is the case in diabetes mellitus with the glucose of urine and blood.

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## STERNAL MARROW IN HEALTH AND DISEASE

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The sternum as a source of bone marrow possesses many advantages:

**Accessibility:** The sternum is a wide, flat, elastic bone and is practically subcutaneous. In the subcutaneous tissue there are no large blood vessels, only a few muscle fibers, and, except in cases of extreme obesity and advanced pregnancy, a small amount of fat. The most important feature, however, is that it contains red marrow of fairly uniform quantity and of low fat content extending from the suprasternal notch to just above the xiphoid.

**Penetrability:** The bone may be pierced with the ordinary spinal needle, although many elaborate needles and drills with various guards have been used. The use of a small hammer has been suggested, but this would probably induce too much psychic trauma.

**Safety:** Due to the width of the sternum and the density of its inner table, there is

little danger of entering the mediastinum while making a sternal puncture. The largest neighboring blood vessels are the mammary vessels which are located laterally about 1 cm. beyond the bone.

The sternum has almost insignificant disadvantages. In children younger than three years, the islands of hematopoiesis are isolated, variable in size and location and difficult to find. In the adult, roentgenograms of the sternum are of no value in determining preferred sites of aspiration because of the shadows of adjacent hard and soft structures. Other bones, such as the rib and tibia, are adjacent to vital structures, or are too resistant to penetration, or contain too much yellow fatty marrow to be suitable for study.

## TECHNIC

One hour prior to the sternal marrow aspiration, the patient is given a rapidly acting barbiturate. The patient is placed on a firm table with no pillow so as to expose the maximum area of the sternum. In hairy-chested individuals the skin over the sternum is shaved. The skin is prepared with weak tincture of iodine and alcohol. With aseptic technic an eye sheet is placed over the sternum with the opening at the desired site. The operator palpates the suprasternal notch to locate the midline, and confirms the location by feeling for the intercostal spaces with the fingers of the opposite hand. The area just below the angle of Louis is the most frequently used because of its conspicuous location. The operator makes an intradermal wheal in the midline with 1 per cent procaine. The procaine is slowly infiltrated into the sternal subcutaneous tissue and periosteum; the latter is very sensitive and requires more anesthetic and time. An area of about 1 cm. in diameter is infiltrated. Most cases require not more than 2 c.c. When the patient experiences no pain on moving the needle over the periosteum, the needle is withdrawn.

The spinal needle with its stylet *in situ* is gently forced through the skin and subcutaneous tissue to the periosteum. Since the bone cannot be anesthetized, the patient

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is told that he will experience a little pain. At this time the needle is supported at two levels: the lower, near the skin, is held with the index finger and the thumb of the left hand to keep the needle from bending, and to prevent the needle from penetrating too deeply or too rapidly; at the upper level the right index finger and thumb are used to twist the hub and push the point through the outer table of the sternum. A "give" comparable to that experienced on piercing the dura in spinal puncture is palpated when the marrow cavity is entered.

As soon as the needle point enters the marrow cavity, the stylet is removed, a 10 c.c. syringe is inserted, and 1 c.c. of the marrow is aspirated. This frequently produces pain and it is advisable to caution the patient not to move. The needle and syringe are removed as a unit, and the contents are gently expelled through the needle into a bottle containing 2 mg. of a previously dried mixture of potassium and ammonium oxalate (Heller and Paul anticoagulant). The bottle is rotated for three minutes to prevent coagulation. Simultaneously, five slides are made from the marrow in the needle. In order to prevent shrinking due to osmosis, the slides are dried rapidly by fanning. From the beginning of aspiration to the deposition of the marrow into the bottle no more than 45 seconds should elapse because of the rapid coagulation of bone marrow.

Light pressure must be applied to the site of aspiration for five minutes after removal of the needle; otherwise there may be a painful hematoma in the subcutaneous tissue of periosteum. No dressing is needed. Within twenty minutes a drop of serum frequently oozes from the skin.

#### LABORATORY PROCEDURES

In the laboratory the bottle is rotated to re-mix its contents well. With a white diluting pipette marrow is drawn to the 1 mark and then diluted with 5 per cent acetic acid containing methylene blue (1 c.c. of 1 per cent methylene blue to 9 c.c. of 5 per cent acetic acid). The acetic acid hemolyzes non-nucleated erythrocytes and leaves the immature erythroid elements as well as the

other myeloid cells clearly defined and conspicuous. The total nucleated elements (T. N. E.) can be estimated by charging an ordinary Levy counting chamber and noting the number of nucleated elements present in five of the central squares (that is, as for the red count). Formula for T. N. E.:

$$\text{T.N.E.} = \frac{\text{Number of cells counted} \times \text{Dilution (10)}}{\text{Area (0.02)}}$$

The megakaryocytes are counted from the fluid remaining in the pipette. After a thorough re-mixing, the fluid is placed in a Fuchs-Rosenthal counting chamber. This counter has a volume of 3.2 cu. mm. and is divided into 256 squares; therefore the following formula is used:

Megakaryocytes=

$$\frac{\text{Number of megakaryocytes counted} \times \text{Dilution (10)}}{\text{Area (3.2)}}$$

The undiluted marrow is next placed in a dry Wintrobe hematocrit tube and centrifuged for five to seven minutes (depending on layer formation) at 2,000 RPM. The marrow divides itself into four layers: (1) a layer of fat which is a pale red or yellow; (2) a layer of clear plasma; (3) the most important layer, composed mostly of nucleated cells and a few erythrocytes (sometimes called the buffy coat); (4) a layer composed of mature red cells and reticulocytes.

When the line of demarcation between the nucleated cell layer and the red cells is not distinct an additional minute of centrifugation will greatly aid separation.

Smears are made from the buffy layer. This concentration of nucleated cells is especially useful in cases of hypoplastic or aplastic anemia.

All slides are stained with Wright's stain. Staining time after dilution is double that used in peripheral blood staining since there is more nuclear material to absorb the stain.

The thin portion of the slide is examined with the high dry lens to note the frequency of the nucleated cells; this also gives a suggestion of the activity of the marrow. Large cells like the megakaryocytes are readily observed. With the oil immersion lens the ratio and stages of development of



TABLE 1  
STERNAL MARROW FINDINGS IN HEALTH AND DISEASE

Diagnosis	Total nucleated elements per c. mm. in thousands	Percentage Distribution				Megakary- ocytes per cu. mm.
		Fat	Plasma	Buffy layer	Red cell layer	
Normal male.....	87.0	3.0	43.0	7.0	43.0	22
Stem cell leukemia.....	150.5	0.0	45.5	22.5	32.0	6
Sickle cell disease.....	207.5	0.0	54.0	20.0	26.0	46
Pernicious anemia.....	47.5	1.7	74.5	6.3	17.5	50

TABLE 2  
STERNAL MARROW IN HEALTH AND DISEASE

Diagnosis	GRANULOCYTES												
	Myeloblasts	Leukoblast	Promyelocytes	Neutrophilic myelocytes	Neutrophilic metamyelocyte	Neutrophiles	Eosinophilic myelocytes	Eosinophilic metamyelocytes	Eosinophiles	Basophilic myelocytes	Basophilic metamyelocytes	Basophiles	Heterophiles
Normal male.....	0.3	1.7	3.9	8.1	12.3	19.3	0.9	1.0	1.9	0.1	0.1	0.1	0.3
Stem cell leukemia.....	0.0	0.0	0.0	0.2	0.3	3.6	0.0	0.1	0.3	0.0	0.1	0.1	0.0
Sickle cell anemia.....	1.7	0.6	1.4	3.7	5.5	8.7	0.1	0.2	1.1	0.2	0.0	0.0	0.3
Pernicious anemia.....	0.4	1.5	2.6	8.3	6.6	22.8	0.1	0.1	0.5	0.2	0.2	0.0	0.1

TABLE 3  
STERNAL MARROW IN HEALTH AND DISEASE

Diagnosis	ERYTHROID SERIES								
	Pronormoblasts	Basophilic normoblasts	Polychromatic normoblasts	Orthochromatic normoblasts	Promegaloblasts	Basophilic megaloblasts	Polychromatic megaloblasts	Orthochromatic megaloblasts	Erythroid mitosis
Normal male.....	0.6	2.1	6.9	16.7	0.0	0.0	0.0	0.0	0.7
Stem cell leukemia.....	0.1	0.3	0.9	2.9	0.0	0.0	0.0	0.0	0.0
Sickle cell anemia.....	2.4	6.9	11.9	34.2	0.0	0.0	0.0	0.0	1.4
Pernicious anemia.....	2.9	4.3	4.1	4.1	4.8	2.4	2.0	1.2	0.8

TABLE 4  
STERNAL MARROW IN HEALTH AND DISEASE

Diagnosis	AGRANULOCYTES								
	Monocytes	Lymphocytes	Immature lymphocytes	Plasma cells	Stem cells	Reticulo-endothelial cells	Damaged cells	Granulocytic lymphocytic erythroid ratio	Peroxidase positive Peroxidase negative
Normal male.....	0.3	9.8	0.3	0.1	0.0	0.3	12.1	5:1:3	1.5:1
Stem cell leukemia.....	0.0	3.5	0.0	0.1	77.1	0.1	9.7	*	1:20
Sickle cell anemia.....	0.0	11.3	0.1	0.6	0.0	0.4	7.2	2:1:6	1:4
Pernicious anemia.....	0.1	13.5	0.2	0.1	0.0	0.8	15.1	4:1:2	1:1

\*Since stem cells are so immature and cannot be positively identified they cannot be classified as myeloblasts or lymphocytes.

the granulocytic, erythroid and lymphoid cells are studied. The cytologic details may be observed but unfortunately the details of marrow architecture are lost. If time is available a differential count should be done using 500 to 1,000 cells.

#### DISCUSSION

Fourteen normal individuals were studied at Charity Hospital to determine the normal marrow findings. The individuals studied were doctors, medical students, and technicians whose ages ranged from 17 to 27 years.

In ten normal males the total nucleated elements varied between 43,000 and 105,000 per cu. mm., and in four normal females the T. N. E. ranged between 30,000 and 87,000 per cu. mm.

The megakaryocytes are large cells measuring approximately 30 micra or more. They may be multinucleated or may possess a multilobular nucleus. There is a large amount of cytoplasm which frequently is surrounded by a clear halo. The total number of megakaryocytes in normal individuals varies from 6 to 22 per cu. mm.; further work on normal counts is being done and will be reported later.

The percentage proportion of the centrifuged marrow as derived from the 14 normal individuals is as follows:

	Per cent
Fat	1 - 3
Plasma	40 - 54
Nucleated elements	3 - 11
Red cells	40 - 51

Tables 1 to 4 exhibit the recommended form for recording the data. The data are derived from one normal individual and typical cases of three blood dyscrasias. All differential counts were made by counting 1,000 cells.

For the beginner the peroxidase stain will be of great aid in cell identification. Cells of the erythroid and lymphoid series are peroxidase negative, and while the myeloblasts and leukoblasts are frequently negative, positive granules are found occasionally. Their fine nuclear pattern will make the final differentiation. Promyelocytes have many peroxidase positive granules and

the remaining cells of the granulocytic series are definitely peroxidase positive. Pronormoblasts and promegaloblasts are peroxidase negative with a fine nuclear pattern and can be differentiated from the myeloblast by their deep blue cytoplasm. The promegaloblast has a greater nucleocytoplasmic ratio than the pronormoblast.

Some authors distinguish between large, medium sized, and small lymphocytes; such a classification is time consuming and does not appear to aid in diagnosis or prognosis. We do not attempt to distinguish on morphological grounds monoblasts or lymphoblasts from myeloblasts, since in our experience the various primitive white cell precursors that have been described by various authors are not sufficiently clear-cut or constant to permit their recognition in smears with any confidence.

#### SUMMARY

The sternum is the site of choice for bone marrow aspiration because of its accessibility, penetrability and safety. The marrow is removed with a spinal needle and is mixed with Heller's oxalate. The total nucleated elements and megakaryocytes are counted from this oxalated marrow. Smears made from the untreated marrow and from the buffy layer are stained with Wright's stain. Tables are furnished citing the sternal marrow findings in a normal individual and in three types of blood dyscrasia.

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### THE "BORROWING-LENDING" HEMODYNAMIC PHENOMENON (HEMOMETAKINESIA) AND ITS THERAPEUTIC APPLICATION IN PERIPHERAL VASCULAR DISTURBANCES\*

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While it has long been known that the

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volume of organs undergoes spontaneous and even rhythmic variations, it was not until the more refined technics of plethysmography became available that a better understanding of these phenomena were obtained. With such technics,<sup>1</sup> studies of a more precise and quantitative nature could be made of these fluctuations in volume in peripheral parts such as the fingers, toes, and pinnae of the ears. These variations in volume have been attributed essentially to changes in the volume of the vascular bed of the part, and thus reflect variations in behavior of the local circulation. As a result of these studies, much valuable information has been obtained concerning the hemodynamics of the peripheral circulation under normal resting conditions, in diseased states, and in response to external and internal stimuli. Although there may be many factors which remain unknown or poorly understood, certain facts have been established which suggest a more rational approach to certain clinical conditions. For these reasons, it seems desirable to present a consideration of these facts and their application to clinical conditions characterized by a disturbance in peripheral circulation.

The plethysmogram may be regarded essentially as an ordinary type of Cartesian coordinate, with the volume represented on the ordinate and time on the abscissa. It is, therefore, a record of the changes in volume of the part enclosed in the extremity cup in relation to time. The recorded volume changes are the algebraic summation of many volume changes, which are taking place in all portions of the enclosed part. Essentially, however, the recorded changes in volume of the part represent variations in the volume of the vascular bed of the part.

By means of plethysmographic studies of this kind it has been shown that the vascular bed in such peripheral parts as the pinnae, the fingers, and the toes undergo spontaneous variations in volume.<sup>1, 2</sup> In the resting individual in a comfortable environment, at least five types of rhythmic changes in volume have been observed. They have been described in detail else-

where and have been given the following designations: (1) *pulse* deflections, (2) *respiratory* deflections, (3) *alpha* deflections, (4) *beta* deflections, and (5) *gamma* deflections. They range in volume from less than 0.1 to 350 or more cubic millimeters per 5 c. c. of part (fig. 1).

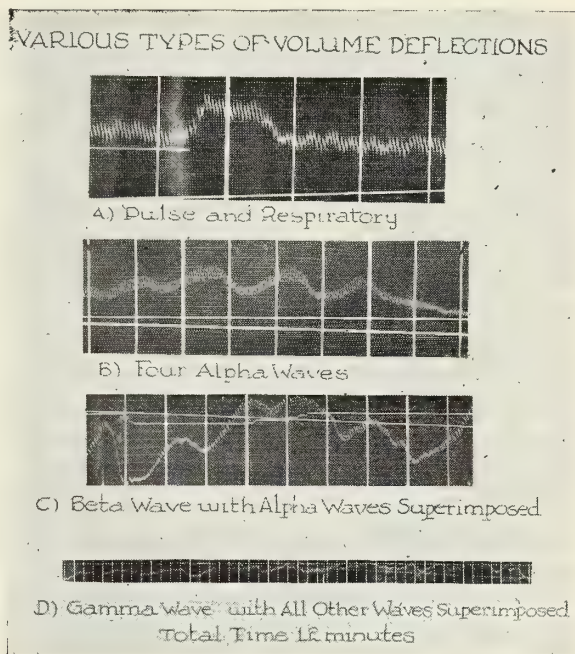


Fig. 1. A. Plethysmogram of a normal subject showing pulse and respiratory deflections. B. Four unusually regular alpha waves. C. Beta wave with alpha waves superimposed. D. A short gamma wave with other waves superimposed. Time, 12 minutes.

The pulse deflections which represent the changes in volume of the part brought about by the blood delivered into the part with each heart beat vary considerably in volume, with mean values of 6.9 cubic millimeters in the finger tips, 4.0 in the toe tips, and 4.1 in the pinnae per 5 c. c. of part.\*<sup>2</sup> The changes in volume are probably due to variations in content of all components of the local circulatory bed; arteries, arterioles, capillaries, venules and veins.

The respiratory deflections represent variations in volume occurring with the normal respiratory cycle and their volumes vary from less than 0.1 to 5 cubic millime-

\* Hereafter all volume changes are expressed per 5 c.c. of part.

ters.<sup>2</sup> They reflect variations in venous return to the heart brought about by respiration. In addition the changes in heart rate and changes in the heart output associated with respiration contribute considerably to the development of these variations in volume.

Alpha deflections occur less frequently than respiratory deflections, usually with smooth contours, but not necessarily uniform. They vary in frequency and size with a tendency for an inverse relationship. The mean frequency has been found to be 7.9 per minute in the finger tips, 7.7 in the toes, and 8.6 in the pinnae.<sup>2</sup> For each of these parts respectively, the mean volumes are 14.5, 7.1, and 6.6 cu. mm.<sup>2</sup> Although independent of variations in arterial pressure,<sup>3</sup> the alpha deflections are predominantly under the control of the sympathetic nervous system, for they almost entirely disappear following interruption of sympathetic pathways.<sup>2</sup> The volume changes represented by the alpha deflections are due essentially to variation in volume of the blood within the part, but their frequency suggests the possibility that variations in lymph volume may be a contributing factor. Experimental studies in animals have shown contractions of the lymphatics to be responsible for much of the flow of lymph.<sup>4, 5, 6</sup> If these lymphatic contractions occur in man and at the same frequency as observed in animals they might contribute to the volume changes.

Beta deflections represent larger and more slowly developing changes in volume upon which alpha waves are superimposed. Their frequency is one to two per minute; the volume varies from 5 to 60 cu. mm.<sup>2</sup> Although they may be irregular in rhythm and volume they tend to vary concordantly in the fingers, toes and pinnae. These deflections are also considered to represent primarily volume changes in the vascular bed, but like the alpha deflections, a significant part of the volume change may be due to variations in lymph volume. Changes in inter- and intracellular volume may also contribute to these deflections.

The gamma deflections are due to still

more slowly developing changes in volume upon which the beta waves are superimposed. Their frequency varies from one to eight an hour and their magnitude from 50 to 350 cu. mm.<sup>2</sup> The gamma deflections are predominantly the result of changes in volume of the vascular bed of the part, although variations in lymph volume probably contribute significantly to the volume change. It would appear that the gamma volume deflections are more likely concerned with large and usually relatively slow shifts in blood volume from one part of the body to another.

Under certain circumstances considerable variations may be found in the plethysmogram of normal individuals. Because these changes may resemble those found in diseased states, it is desirable to review them briefly. Among the factors which may produce these changes are the psychic state of the individual, the temperature of the environment, the relation of the part to heart level, and the presence or absence of intact sympathetic pathways to the part.

The psychic state of the individual has a profound influence upon the pulse and alpha deflections. For example, fear, anxiety, or tenseness on the part of the individual tend to produce a diminution in the pulse and alpha deflections and an increase in the rate of the pulse deflections.<sup>7, 8</sup> This is apparently due to an increased sympathetic activity associated with the psychic disturbance, causing an increase in vasomotor tone. The character of the spontaneous volume deflections may thus serve as a good reflection of the psychic state of the individual.

The environmental temperature may also produce marked changes in the spontaneous volume deflections. For example, chilling of the subject, either by local application or general environmental cold produces vasoconstriction and a consequent reduction in the volume of the pulse and alpha deflections and a decrease in the total volume of the part (negative gamma deflection). In general the degree of vasoconstriction is proportionate to the degree of chilling. On the other hand, a warm environment has



the reverse effect, producing a vasodilatation and a consequent increase in the volume of the pulse deflections. As the part warms, the alpha deflections are increased. Later, after full vasodilatation there is a decrease in the alpha deflections. The positive gamma deflection which follows warming the subject indicates an over-all increase in the volume of the part. As has been indicated previously, these reactions serve as a good test for organic occlusive arterial and arteriolar disease.<sup>1</sup> In the presence of these conditions, such as thromboangiitis obliterans or obliterating arteriosclerotic endarteritis, these vasodilating responses are impaired or absent. The effort to produce vasodilatation in the fingers or toe tips by the application of heat to another extremity tests the patency of the blood vessels to the part under investigation as well as the neurovascular mechanism of the part.

The position of the part in relation to heart level also affects these spontaneous volume deflections. Placing the part below heart level, for example, produces a decrease in the volume of pulse and alpha deflections. The pooling of blood and lymph in the dependent part as a result of gravity causes a positive gamma deflection. Two factors, either alone or in combination, have been suggested as a means of explaining this phenomenon. The first is arteriolar vasoconstriction and the second, which is more likely, is distention of the vessels secondary to increased venous pressure, with a diminution in further distensibility of the vessel wall.<sup>9</sup> Elevation of the part above heart level produces the reverse effect. There is pronounced increase in the volume of the pulse and alpha deflections and as a consequence of the draining out of the blood within the part, a negative gamma deflection. For these reasons, the part should be kept at or near heart level for standard recordings.

The spontaneous volume deflections are greatly affected by the state of the sympathetic pathways to the part. Thus, within a few minutes after the regional sympathetic nerves or ganglia have been blocked

by infiltration with 1 per cent procaine hydrochloride solution, there is a marked increase in the volume of the pulse deflections and virtual disappearance of the alpha deflections. The engorgement of the vascular bed within the part following the sympathetic block also produces a large positive gamma deflection. The procedure of sympathetic block is another significant diagnostic test,<sup>10, 11</sup> for by this means it is readily possible to determine the degree of the normal, or, in certain conditions, the abnormal sympathetic vasoconstrictor tone and the extent of vasodilatation or the general order of the amount of increase in vascularity of the part that can be achieved by interruption of these pathways.

#### THEORETICAL CONSIDERATIONS OF THE "BORROWING-LENDING" HEMODYNAMIC PHENOMENON (HEMOMETAKINESIA)

In addition to the spontaneous variations in the volume of the vascular bed of such peripheral parts as the fingers, toes, and pinnae, which are represented on the plethysmogram by the alpha, beta, and gamma deflections, similar variations in the volume of certain internal organs have been demonstrated. For example, Richards and Schmidt<sup>12</sup> observed an intermittent blood flow through kidney glomeruli and Krogh<sup>13</sup> made similar observations in the tongue and skeletal muscles of the frog. The irregularities in the blood flow in the rabbit's ear were also reported by Grant.<sup>14</sup> Further experimental observations by Zweifach<sup>15</sup> and Chambers and Zweifach<sup>16</sup> on the circulation in various organs have demonstrated clearly the intermittency of blood flow in different parts of the body, a phenomenon which they termed vasomotion. The spontaneous variations of the splenic volume in the dog, reported by several observers,<sup>17-21</sup> are of a magnitude and frequency comparable to those of the beta and gamma deflections described above.

It is readily evident from these considerations that spontaneous variations in the vascular bed of different parts of the body are constantly occurring. These changes in the volume of blood in widely separated parts of the body may be rhythmic, concordant, or discordant. They may be pro-

duced by intrinsic factors, which are not yet well understood, or may be influenced by various internal and external stimuli. They indicate a continuous shifting back and forth of the blood from one part of the body to another to meet local requirements.<sup>22</sup> They suggest a well regulated mechanism, with definite order and significance, which appears to be concerned with certain vital functions such as proper thermal regulation, nutrition, repair, and other important physiologic adjustments.

It is conceivable that at least a part of this significance lies in the attempt by the body mechanism to utilize its total blood volume in the most efficient manner. Obviously the total volume of blood in the body at any one time is too small to meet the maximum demand of all the tissues at the same time, should a disease state arise to precipitate such a situation. The total blood volume, on the other hand, is more than sufficient to meet urgent demands for large quantities of blood in isolated parts. While great variations can take place in the vascular bed within a relatively short period of time, especially in isolated parts of the body, the total blood volume remains relatively constant under ordinary conditions. For example, the vascular volume of a finger or toe can be observed to double in size within a matter of minutes. To fill this augmented vascular bed with blood, however, obviously does not require doubling the total blood volume nor is there reason to believe that there exists in the body a special reservoir of blood for this purpose. Yet, it must have come from some source and the obvious explanation is that it was taken from the vascular bed of other parts of the body. In other words, the total blood volume need not be changed by even one cubic centimeter. The only change required to achieve this purpose is an adjustment in the vascular bed. By increasing the volume of the vascular bed in one part of the body and decreasing it by the same amount in other parts, the volume of blood in the former area is increased at the expense of the latter without any variations in the total volume of the blood.

To illustrate this "borrowing-lending" phenomenon (hemometakinesia), the following observations are presented. These data have been selected from many similar experiences in normal individuals as well as patients with various forms of peripheral vascular disease. The results of these studies have been invariably consistent, regardless of the methods employed to determine and record variations in blood flow. Our experiences include particularly the use of thermometric and phlethysmographic methods of study. These observations are routinely made under controlled atmospheric conditions in a room constructed to reduce psychic disturbances. The subjects rest in bed for a time sufficient to permit stabilization of the vascular system. Plethysmograms are obtained for the distal phalanges of the fingers and toes, and for the pinnae of the ears. The index finger and the second toe are most commonly employed. Thermograms are obtained for these parts as well as others distributed bilaterally and symmetrically over the body, a total of twenty areas usually being observed. The plethysmographic and thermometric observations are usually made simultaneously. The response to various measures, such as interruption of sympathetic innervation, reactive hyperemia, drugs, environmental and local temperature changes, and psychic and neurogenic factors are observed as reflections in the plethysmograms and thermograms.

#### CASE NO. 1

G. I., a white male 17 years of age, was examined because of marked hyperhidrosis. Plethysmographic and thermometric studies were made after the patient had rested in bed in the observation room (room temperature 78° F. and relative humidity 46 per cent) for 50 minutes. Skin temperature determinations were made bilaterally on the third toe, the dorsum of the foot, the mid-pretibial area, the knee, the mid-thigh and the chest. The plethysmographic determinations were made for the distal phalanges of the right index finger and for the second toe bilaterally. After the patient had reached a state of stabilization 500 mgm. of tetraethyl ammonium chloride<sup>23</sup> were injected intravenously. Then after sufficient time had elapsed for the reaction to subside a left lumbar sympathetic nerve block was performed with 1 per cent procaine hydrochloride solution. The vascu-



## Studies in Peripheral Vascular Responses

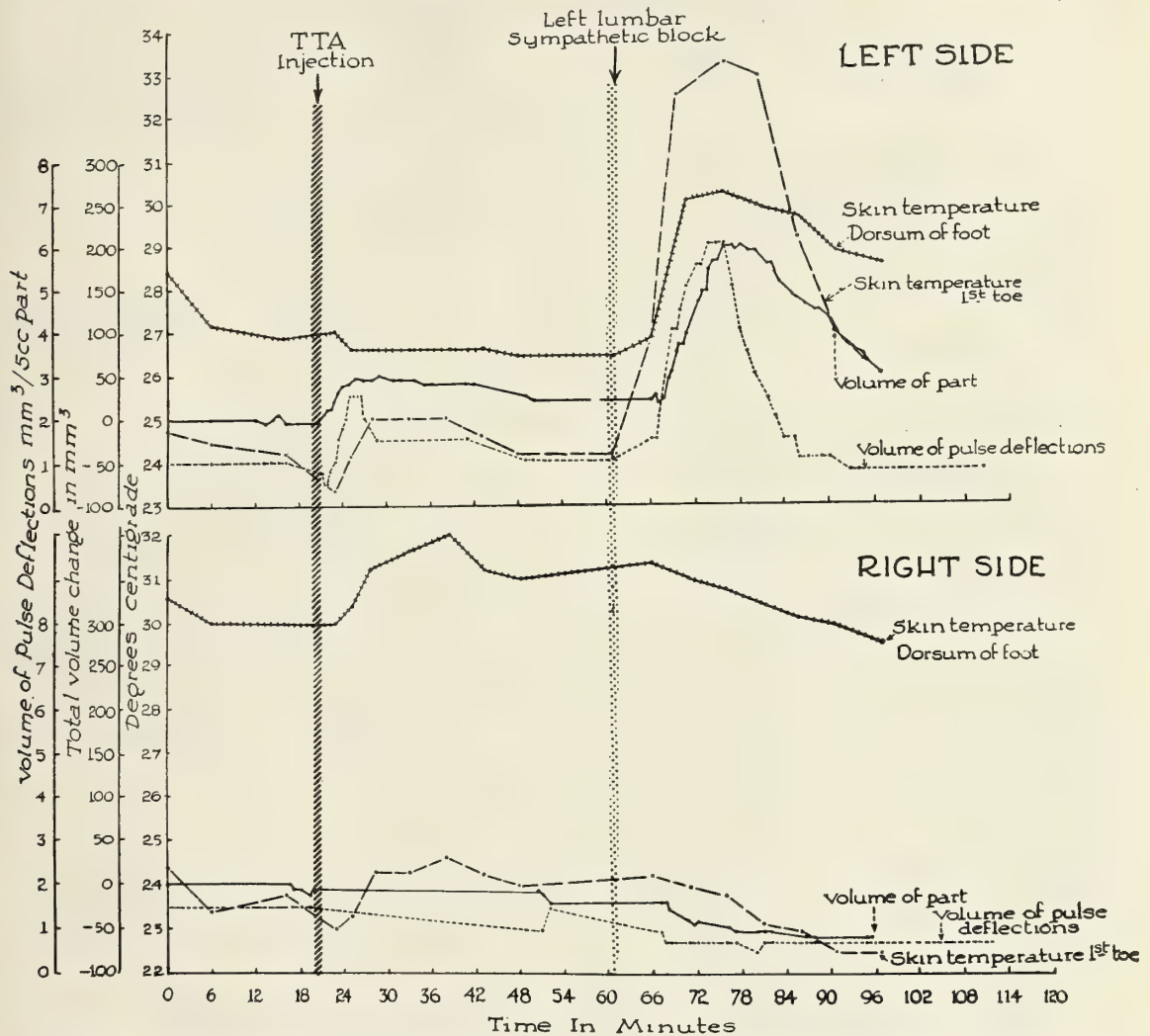
Room Temp. 78°F.  
Relative Humidity 46%

Fig. 2. Graph showing thermometric and plethysmographic response following injection of tetraethyl ammonium chloride (T.T.A.) and left lumbar sympathetic block. See text for details.

lar phenomena resulting from these procedures are shown in figure 2.

Initially the patient was stabilized in a state of moderate vasoconstriction as evidenced by: (1) small pulse deflections; (2) small fluctuations in the total volume of the part; (3) relatively low skin temperature of the toes.

The procedure of intravenous injection of tetraethyl ammonium chloride resulted in a further vasoconstriction as evidenced by a decrease in the volume of pulse deflections. Following the injection of tetraethyl ammonium chloride there was a slight vasodilatation shown by an increase in the volume of pulse deflections, an increase in the total volume of the part and a rise in skin temperature. These reactions were slight. There were skin temperature changes on the right side of the same magnitude as on the left but no determina-

tions of pulse deflections and total volume were made in the right toe during this period.

Within a few minutes after the left lumbar sympathetic block was done the following phenomena were observed:

1. A rapid elevation of the skin temperature of the left leg with marked flushing and an absence of sweating.
2. An increase in the volume of the pulse deflections of the left second toe.
3. An increase in the total volume of the left second toe.
4. A fall in the skin temperature of the right leg.
5. A decrease in the volume of the pulse deflections of the right second toe and index finger.
6. A decrease in the total volume of the right second toe and index finger.

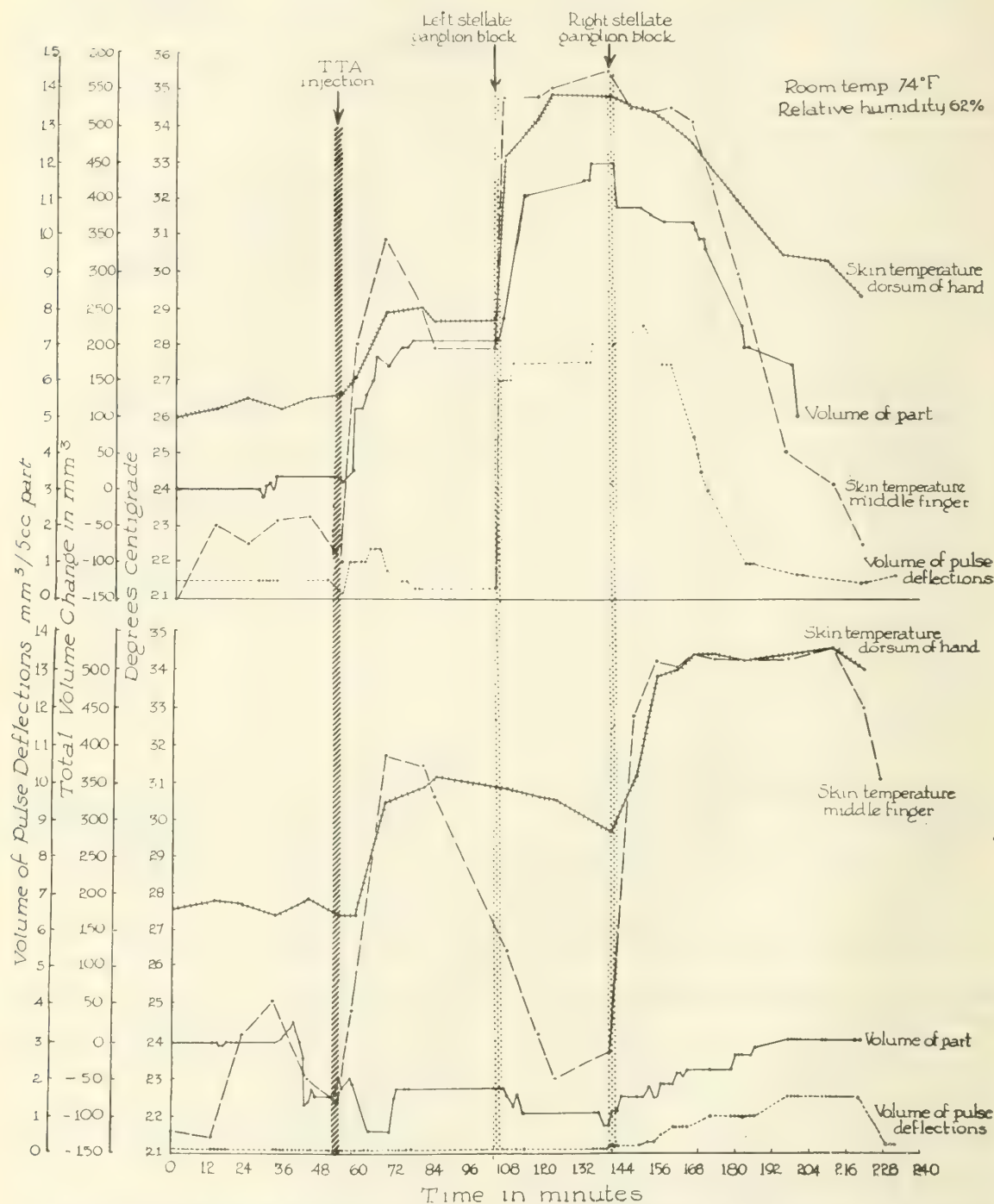
Studies in Peripheral Vascular Responses

Fig. 3. Graph showing thermometric and plethysmographic response to injection of tetraethyl ammonium chloride and left and right stellate ganglion block. The upper half is the left side, the lower half is the right. See text for details.

These changes indicate a vasodilatation in the left leg. There was an increase in the volume of blood and rate of blood flow to this leg which occurred at the expense of the vascular bed of the remainder of the body. That blood was borrowed

from the remainder of the body is evidenced by the fall in skin temperatures, the fall in total volume and volume of pulse deflections in all other areas. The magnitude of changes observed in the areas which were concerned with "lending" were small,



indicating that the remainder of the vascular bed and not any one single area is involved. The normal physiologic adjustments are such that no one organ or tissue is called upon to give up its blood to an extent which would produce injury as a result of ischemia. The previous state of vasoconstriction or vasodilatation will determine in large part the degree of lending possible. As demonstrated in this subject, a part which is already in a state of vasoconstriction (the right toe) can not give up as much blood as would be expected of a part in mid or full vasodilatation.

#### CASE NO. 2

A.M., a white male aged 59, suffered from arteriosclerosis and Raynaud's phenomenon. After resting in bed for 60 minutes in an environmental temperature of 74° F. and 64 per cent relative humidity the following studies were made; these included a measurement of skin temperatures of the first toe, dorsum of the foot, mid-pretibial area, knee, mid-thigh, chest, deltoid region, forearm, dorsum of the hand and middle finger bilaterally as well as plethysmographic studies of the right second toe, the left index finger and the right fourth finger. The latter was selected instead of the right index finger because of the more severe cyanosis which the fourth finger presented.

After a state of stabilization had been reached, 5 c.c. (500 mgm.) of tetraethyl ammonium chloride were given intravenously. Fifty minutes later a left stellate ganglion block was performed with 1 per cent procaine. Then after another 35 minutes the right stellate ganglion was blocked in the same manner.

Initially the right ring finger was cyanotic and the entire right hand presented a mottled cyanotic appearance. The left index finger was cyanotic but not as marked as the right fourth finger. The initial skin temperatures were low on both sides and the pulse deflections were small. Following the injection of tetraethyl ammonium chloride the skin temperatures of both hands increased significantly. There was an increase in the total volume of the left index finger and a small increase in the pulse deflections. The right finger did not show pulse or volume changes. Coincident with the increase in temperature the skin color improved but did not reach normal. Cyanosis returned before the left stellate ganglion block was performed.

Immediately following the left stellate ganglion block the following phenomena were observed (fig. 3):

1. An immediate rise in skin temperature of the left arm and hand with the most pronounced changes distally.
2. A flushing of the left arm and hand with a return of normal skin color.
3. A pronounced increase in the pulse deflections.

4. A marked increase in the total volume of left index finger.

5. A decrease in the skin temperature of the right arm and hand.

6. A decrease in volume of the right finger.

7. An increase in the degree of cyanosis of the right finger.

Immediately after the right stellate ganglion block the following changes were noted:

1. A marked increase in skin temperature, again most pronounced distally.

2. Disappearance of the cyanotic color.

3. A significant increase in the volume of the pulse deflections.

4. An increase in the total volume of the right finger.

5. A decrease in skin temperature of the left arm and hand.

6. A decrease in the total volume and the volume of the pulse deflections of the left finger.

7. Reappearance of a mottled cyanotic skin color in the left hand.

Terminally, the volume of the pulse deflections decreased in the right finger and the cyanosis reappeared.

The changes observed in this subject indicate vasodilatation following injection of tetraethyl ammonium chloride. Following the left stellate ganglion block there was an increase in the volume of blood and the rate of blood flow in the left arm. This increase in the left side is indicated by the rise in skin temperature, total volume and volume of the pulse deflections. That this occasioned a "lending" from the right arm is evidenced by a decrease in skin temperature and total volume. The volume of the pulse deflections on the right was very small and could not be diminished any further. The preexisting state of the right finger precluded its lending but a very small amount of blood without danger of ischemia. The increase in cyanosis could be interpreted as a deleterious effect—an actual deprivation below the very minimal needs for viability of the tissues.

Immediately after the right stellate ganglion block there was vasodilatation in the right upper extremity. This is shown by the occurrence of the same changes demonstrated in the left arm when the left stellate ganglion was blocked. The cyanosis on the right side disappeared. However, when the shift of blood began toward the right arm the left was in a state of marked vasodilatation. It, therefore, was able to "lend" more blood than was possible for the right arm previously. That this is precisely what occurred is shown by the marked decreases in skin temperature, total volume and volume of pulse deflections in the left side as compared to the small changes which occurred previously with a small "loan" from the right to the left arm.

## DISCUSSION

From the foregoing considerations, it seems evident that there is a continuous shifting back and forth of blood from one part of the body to another. It is suggestive of a borrowing and lending of blood, a phenomenon for which we should like to suggest the term "hemometakinesia." This borrowing and lending of blood from tissue to tissue, to meet variations in requirements is indicative of a well regulated mechanism which permits the body to utilize its limited total blood volume in the most efficient manner. The essence of this mechanism lies in the control and regulation of the vascular bed. By this means, adjustments in the vascular bed can be made to permit an increase in the volume of blood in one part of the body with a corresponding simultaneous decrease in the volume of blood in other parts of the body. Thus, the blood flow to different parts of the body may be varied considerably without affecting the total blood volume or cardiac output.

It is well to point out that when blood is borrowed from any organ, this blood is removed from all blood vessels of the organ. A larger part, however, must come from the large vessels within the organ, such as the venous reservoirs. The relative contributions made by the small vessels are unknown. From the studies of others<sup>24</sup> the small vessels would be expected to contribute a relatively small portion.

In approaching therapy designed to increase the local circulation to a part, such as in peripheral vascular disease, the application of similar principles of hemodynamics appears rational. These conditions are characterized by a disturbance or an actual diminution in the normal amount of circulating blood to a part. Effective therapy is aimed at improvement in the circulation or increase in blood supply to the part. According to the principles of hemodynamics described above, it would not be advisable even were it possible to achieve this purpose by therapeutic measures designed to produce dilatation of the entire vascular bed, when a diseased state is localized to a single peripheral part. Nonetheless, medical

literature is replete with articles reporting studies and claims for agents directed at local therapy through the production of generalized vasodilatation. Should such an agent, with the ability to produce maximum generalized vasodilatation, exist and be employed, the reaction would be shock-like, completely defeating the original purpose of increasing the blood supply to a local part. This becomes readily evident when it is realized that should the entire vascular bed suddenly increase greatly in volume, a great disproportion would immediately occur between the volume of the vascular bed and the available volume of blood. With a relatively fixed total blood volume, it would be impossible to increase the circulating blood volume in any one single part or tissue if there were a comparable increase in the volume of the entire vascular system. Furthermore, if the volume of the entire vascular bed increased suddenly, the drop in intravascular pressure or blood pressure would be so great, that the blood flow in a localized part would be impaired rather than improved. It seems evident, therefore, that therapeutic measures designed to provide the maximum increase in the blood supply to a local part, through the medium of a generalized vasodilatation, is theoretically unsound.

On the other hand, therapeutic measures having as their purpose the production of local vasodilatation limited essentially to the part in need of more blood, is theoretically sound and potentially effective. In our experience, this is best accomplished by sympathetic denervation of the affected part. This therapeutic approach conforms with the principles of hemodynamics described above and provides the maximum local vasodilatation which is possible in a given case without reducing the arterial blood pressure or producing serious systemic disturbances in hemodynamics by the sudden creation of a disproportion between the total volume of the vascular bed and the total volume of blood. Theoretically there should be, and actually, as is illustrated by the case described above, there has been found to be a definite and significant in-



crease in blood supply to the diseased part by this form of therapy. In fact, we have yet to find a general vasodilator agent, which could produce in a local part, such as the toes, fingers, foot, hand, or an entire extremity, vasodilatation equal in degree or duration to that produced by sympathetic denervation of the part.

## SUMMARY

Although some phenomena of the peripheral circulatory reactions may not be completely understood, the facts which have been established indicate that there is a continuous shifting of blood from one part of the body to another. This "borrowing and lending" indicates a well regulated mechanism which permits the body to meet the marked variations in local requirement of blood with a limited total blood volume. The underlying principle is a control of the vascular bed which permits an increase in the volume of blood in one area with a simultaneous decrease in other areas. In this manner the total blood volume is unaltered.

For this "borrowing-lending" mechanism the term *hemometakinesia* is proposed.

It is suggested that this hemodynamic principle is applicable in the management of peripheral vascular diseases in which the aim of therapy is an increase in the blood supply to the part. Measures which are directed toward improvement of the local circulation by the production of generalized vasodilatation are of doubtful value and not in conformity with the natural physiologic mechanism. However, sympathetic denervation, the most effective method of increasing local blood supply, is in complete conformity with the concept of hemometakinesia.

Two cases are presented to illustrate the "borrowing-lending" phenomenon and to demonstrate the value of sympathetic denervation as a therapeutic measure in peripheral vascular disease.

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## THE TREATMENT OF UTERINE PROLAPSE\*

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In the writings attributed to Hippocrates<sup>1</sup> in the fourth century B. C. is an excellent description of complete uterine prolapsus, in which he advises washing the parts with black wine, manual reposition, and seven days' rest in bed with the feet elevated. No mention is made, however, of the end results of this procedure.

Soranus,<sup>2</sup> of Ephesus, of the second century A. D., is our leading authority on the obstetrics and gynecology of the ancients. Even in that day, perineal bandages and pessaries were looked upon as time-honored methods of treatment. Soranus chides Euphyron for suspending his patients by the feet to a ladder for a period of 24 hours, and scores those who believed that the prolapsed uterus would retreat to its natural position if exposed to evil-smelling medications. He advocated manual replacement, binding the legs together, and, after several days' rest, use of a pessary of wood dipped in myrrh.

Little if any progress was made in the treatment of uterine prolapse during the middle ages, or in the Renaissance, for we find that during this time Rodericus a Castro<sup>3</sup> attacked the procidentia with a red hot iron to cause it to retreat into the vagina, while others bound lizards and mice to the uterus to frighten it into normal position. Paré<sup>4</sup> advised the use of a pessary consisting of a ball covered with leather, but does not mention surgery for the correction of the condition.

In 1702, Stephen Blancard<sup>5</sup> inferred surgical treatment of prolapse in his definition of "Procidentia Uteri" in *The Physical Dictionary*:

"A relaxing of the Inner Tunick of the Womb, which falls through the Privities and was cut off by Physicians."

The first suggestion of a rational surgical approach to treatment of prolapsus is attributed to the French surgeon, Romaine Gerardin,<sup>6</sup> who, in 1823, proposed obliteration of the vaginal orifice by suture of the denuded labia. He did not, however, perform the operation. Eight years later (1831) Marshal Hall,<sup>7</sup> of London, proposed a rectangular denudation of the anterior vaginal wall followed by side-to-side suture of the denuded area in such a manner that the prolapsed uterus would be supported by the narrowed vagina. Heming<sup>8</sup> followed Hall's suggestion and performed the operation with success in 1931.

Shortly thereafter, Geddings<sup>9</sup> is credited with first combining perineorrhaphy with narrowing of the vaginal walls. Judging from the description of these early operations and from the accompanying illustrations, the operators depended almost entirely upon suture of the mucosa and skin. The deeper supportive structures were not repaired, and, in most instances, the operation served only to narrow the vaginal orifice, so that a ring pessary could be utilized. Important contributions were made to vaginal plastic surgery by Diffenbach, Velpeau, Marion Sims, Emmet and others during the middle of the nineteenth century. In 1877 Leon LeFort<sup>10</sup> advocated partial occlusion of the vagina by suturing together the denuded anterior and posterior vaginal walls. Almost simultaneously Neugebauer,<sup>11</sup> in Germany, devised much the same operation, which, with little modification, is now found useful in a definite but small group of cases.

In 1888, Donald,<sup>12</sup> of Manchester, England, then senior resident surgeon in St. Mary's Hospital, devised the combination of anterior and posterior colporrhaphy with amputation of the cervix, and called particular attention to the necessity of suture of the bases of the broad ligaments anterior to the cervix. This procedure was later modified by Fothergill<sup>13</sup> and more recently by Fletcher Shaw,<sup>14</sup> but with little change, the Manchester operation constitutes today the most effective treatment of the majority of cases of uterine prolapse.

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In the choice of treatment for uterine prolapse, patients must be individualized by consideration of many pertinent factors. Age, general condition of the patient, degree of prolapse, sexual life, the desire for additional children and other associated pelvic disorders constitute the chief points on which the decision must be based.

In most instances, surgical repair of the torn or attenuated supportive structures constitutes the procedure of choice. On the other hand, since procidentia occurs more often in elderly women, a considerable number are poor operative risks. For the treatment of this group, some form of mechanical support must be used. Conservative treatment is indicated also in younger women with partial prolapse, who desire to postpone extensive repairs until additional children are borne; similar measures are applicable to the occasional cases of prolapse which occur during pregnancy.

Circular hard rubber pessaries are preferable to the soft or sponge rubber type, as the latter, being rough, readily become encrusted with secretion, are foul in odor, and are more irritating to the vaginal wall. The caliber of the hard rubber pessary should be as small as will maintain the uterus and the associated cystocele in proper position. Ring pessaries of the same caliber rubber as the usual Smith pessary accumulates less encrusted mucus and permit better drainage than those made of larger caliber material. The ring pessary should be large enough in diameter to fill the relaxed vagina and rest comfortably against the pubic rami without making undue pressure on the lateral vaginal walls or the urethra. Occasionally, the vaginal orifice is too small to allow the insertion of a ring large enough to support the uterus; in such cases the collapsible soft rubber pessary must be used despite its disadvantages.

Tampons are useful in maintaining the completely prolapsed structures in position while treating decubitus ulceration of the cervix in preparation for operation. In rare instances, tamponage may prove to be the only method applicable to an elderly patient whose pelvic floor is too relaxed to

hold a pessary in place; continued use of tampons, however, has the disadvantage of macerating the atrophic vaginal epithelium.

The cup-pessary with its attached stem and harness is rarely justifiable. With this device in place, the entire weight of the uterus rests on the cervix, and decubitus ulceration is almost inevitable. Some few patients, who cannot be subjected to operative repair, and who, for various reasons, cannot be fitted with any mechanical support, find considerable relief from the use of a vulvar pad with a tightly applied perineal binder.

#### SURGICAL TREATMENT

Every gynecologist has his favorite operative methods for correction of uterine prolapse. No one method is suited to all cases, but certain principles are common to all successful operations. The chief cause of prolapse is, unquestionably, over-stretching or tearing of the fibromuscular supportive tissue in the bases of the broad ligaments. Therefore, any procedure which does not include shortening of these structures is doomed to failure. In addition, the almost invariably associated cystocele and rectocele must be repaired, and attention must be given to the frequently associated enterocele.

#### MANCHESTER OPERATION

This procedure consists of amputation of the cervix, shortening of the bases of the broad ligaments, and anterior and posterior colporrhaphy. The details of the technic of this operation have been so well presented by Fletcher Shaw, of Manchester, and more recently by Frank, Gordon, and Curtis in this country, that there seems no necessity to do so in this presentation. The order in which this combination of procedures has proved most effective and, in our hands, easiest to perform, is as follows: elevation and suture of the bladder high on the anterior face of the uterus, amputation of the cervix, covering the posterior lip of the cervix with Sturmdorf's stitch, cutting away the excess vaginal mucosa, placing but not tying the broad ligament sutures anterior to the cervix, completion of the cervical covering, closure of the anterior colporrhaphy

from the urethral end, and finally tying the sutures previously placed through the bases of the broad ligaments. We have found that tying these chief supportive sutures earlier in the operation often elevates the cervix to such a degree that the remainder of the anterior closure is rendered extremely tedious. Posterior colporrhaphy completes the operation. This is the least radical of all the major surgical measures and is, therefore, best suited to the young woman who desires to have additional children. Shaw found in his follow-up study that labors subsequent to this operation were well tolerated; in only 18.5 per cent was there any recurrence of symptoms. Another advantage is that vaginal depth is more regularly conserved in this procedure than in the more radical measures. The Manchester operation is my choice also for partial prolapse in older women, if there be no special indication for hysterectomy. The shortening of the bases of the broad ligaments may be accomplished with or without detaching them from the sides of the cervix. If the cervical amputation is high, I prefer to detach them and bring them together anterior to the cervix; if the amputation is low, simply overlapping the unsevered ligaments anteriorly serves the same purpose and gives a less "bunchy" anterior cervical lip.

#### THE INTERPOSITION OPERATION

This procedure was devised in 1898 almost simultaneously by Thomas Watkins<sup>15</sup> and by Wertheim.<sup>16</sup> It consists of longitudinal incision of the anterior vaginal wall in the plane between the bladder and the vesicovaginal layer of the endopelvic fascia, elevation of the prolapsed bladder beyond the line of the peritoneal reflection, incision of the peritoneum of the anterior cul-de-sac, extraction of the fundus of the uterus through this opening, suture of the top of the fundus to the fascia just under the pubic rami, and closure of the anterior vaginal wall so that the base of the bladder rests on the posterior surface of the uterus. Posterior colporrhaphy completes the operation.

Because of the distorted relations of the uterus and the bladder, childbirth after this procedure is hazardous, if, indeed, it is possible. The operation should, therefore, be utilized only after the menopause or artificial sterilization. Its field of greatest usefulness is in elderly women with cystocele and only partial prolapsus. We do not use this procedure in any case in which the cervix protrudes more than one inch beyond the vaginal orifice. The operation in our hands is poorly adapted to the correction of complete prolapse because the relaxed uterosacral ligaments in these cases fail to maintain posterior traction on the cervix. Unless the cervix is held well back in the pelvis, recurrence of the procidentia not infrequently occurs. Care should be exercised that the fundus be sutured firmly enough under the pubic rami to fill the hernial orifice through which the cystocele pushed its way.

The interposition operation is not used in our clinic in young women who are sexually active, because of the high incidence of postoperative dyspareunia.

#### VAGINAL HYSTERECTOMY

Removal of the uterus is not practiced in our clinic in cases of partial prolapsus unless there be some indication for hysterectomy other than malposition of the uterus. The uterus is the keystone of the upper pelvic arch, and its removal renders shortening of the broad ligaments more difficult. Vaginal hysterectomy is, therefore, rarely utilized electively except in occasional cases of complete prolapse in elderly women.

A brief outline of our procedure is as follows: transverse incision of the vaginal wall just anterior to the cervix; blunt dissection of the bladder from the vaginal wall; longitudinal incision of the anterior vaginal wall from the cervix to a point near the external urinary meatus; elevation of the bladder above the point of peritoneal reflection; completion of circular incision of vaginal mucosa into posterior cul-de-sac; clamping and ligation of both uterosacral ligaments and the lower half of both broad ligaments; severing these ligaments from the uterus; incision of the anterior cul-de-sac, with the



finger in the peritoneal cavity as a guide; delivery of the fundus through the anterior peritoneal opening; ligation of the upper half of both broad ligaments; excision of the uterus; purse string closure of the peritoneal cavity; uniting the severed broad ligaments in the midline; anchoring the united upper ends of the broad ligaments to the fascia under the pubic rami (Mayo technic), just as the uterus is anchored in the interposition operation; attaching the vaginal vault to the united bases of the broad ligaments; anterior and posterior colporrhaphy.

Attention should be directed to the possibility of an associated enterocele, and, if present, the hernial sac must be obliterated or removed. In performing the anterior colporrhaphy on those patients who are incontinent of urine, two or three mattress sutures are taken in the fascia underlying the internal urinary meatus. These sutures should be firm, but should not unduly constrict the urethra; tight constriction often delays the return of normal sphincteric action and prolongs the necessity of catheterization.

#### PARTIAL COLPOCLEISIS

Partial closure of the vagina by LeFort's operation is the simplest of all the surgical procedures for the correction of complete prolapse. Since, on completion of the operation, the vagina is practically closed, it is limited in its applicability to those patients whose sexual life is of no importance. It is easily performed under local anesthesia; little, if any shock attends the procedure, postoperative complications are rare, and the final results, in the limited number of patients to whom we have found the operation suited, have been eminently satisfactory.

After excluding, by curettage, the possible presence of fundal malignancy, the first step of the operation is a rectangular denudation of the anterior vaginal wall. The denuded area should not be more than 4 centimeters wide, and should extend from a point just below the cervix almost to the urethral orifice. A similar denudation of the posterior wall is followed by a suture of

the edges of these identical rectangles, beginning just below the cervix and proceeding toward the introitus. The sutures are placed in pairs, one on each side, so that, as the operation proceeds, the cervix disappears and the prolapsed uterus gradually returns to its normal level. Firm perineorrhaphy is essential for proper support. On completion of the operation, a narrow channel extends upward from each side of the vaginal orifice and these are continuous with the transverse channel just below the cervix. This channel must be of sufficient caliber to provide adequate drainage of cervical and uterine secretions.

The foregoing constitutes our general ideas of the indications for the various operative procedures for the treatment of prolapsus. A brief analysis of 50 consecutive personal cases might be of value in indicating the relative frequency of utilization of the various methods. These, rather than service cases, were chosen because they obviously represent more accurately my own ideas of the subject. The group consists of 24 cases in which the cervix presented at the vaginal orifice and 26 in which a part or all of the uterus protruded beyond the introitus. Lesser degrees of descensus have not been considered in this summary.

The Manchester operation was done in 29 cases and the result was entirely satisfactory in all but two cases in which partial incontinence of urine has persisted.

Vaginal hysterectomy was done in eight cases. In three of these, functional uterine bleeding constituted the indication for removal of the uterus and in one an associated carcinoma of the fundus was similarly treated. The other four hysterectomies were performed electively on elderly patients with complete prolapsus. The results were uniformly satisfactory.

The interposition operation was used in six women in whom the cervix did not protrude beyond the vaginal orifice. The results in this small group have been good.

Partial colpocleisis under local anesthesia, by the LeFort technic, was utilized in seven elderly widows, whose age and general condition contraindicated a longer and more

anatomic surgical procedure. One patient in this group died suddenly while walking in the ward on the seventeenth postoperative day, apparently of cardiac dilatation. The other six patients have been completely relieved.

In closing this brief discussion of the treatment of uterine prolapse, I should like to reiterate that no one method can apply to all cases, and that proper choice of treatment for any patient can be made only after evaluation of many factors.

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### SIGMOID SINUS THROMBOSIS

#### REPORT OF A CASE\*

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NEW ORLEANS

AND

WM. W. HART, M.D.

SHREVEPORT

The case presented is one of sigmoid sinus thrombosis which developed as a com-

plication of an acute exacerbation of long standing chronic suppurative otitis media.

#### REPORT OF CASE

A 22 year old negro man was admitted to Charity Hospital in New Orleans September 1, 1946, complaining of severe shaking chills, high fever and pain in the left ear. He gave a history of chronic, foul, purulent discharge from the left ear for seventeen years. Four days prior to admission to the hospital the otorrhea stopped and the ear became painful. Within 24 hours the patient had a severe shaking chill and high fever. He had two additional chills and exhibited a septic temperature. The otorrhea on the left recurred one day before the patient was admitted to the hospital.

On admission to the hospital the patient was acutely ill. His temperature was 104.4 F. (fig. 1). The copious, purulent discharge filled the left external auditory canal. The ear drum was obscured by granulation tissue polyps. There was neither postauricular swelling nor obliteration of the postauricular fold. However, exquisite tenderness was found over the mastoid antrum and this extended posteriorly over the sigmoid sinus, suggestive of a perisinus abscess. Palpation revealed deep tenderness in the neck along the left internal jugular vein. There was moderate nuchal rigidity but no other evidence of meningeal irritation. Neither nystagmus nor past pointing could be found. Weber's test showed lateralization to the left ear; the result of the Rinne test on the left was negative.

Examination of the blood revealed 15,000 white blood cells per cubic mm. of blood with 87 per cent polymorphonuclear leukocytes. No malarial parasites were found. Blood cultures gave negative results on September 5 and 6. Examination of the spinal fluid on admission disclosed no increase in pressure, clear fluid and no cells. The sugar was 74 mg. per cent and chlorides 655.2. The Tobey Ayer test was not done. The only other abnormal finding was a soft blowing systolic precordial murmur. The electrocardiogram was normal.

A tentative diagnosis of sigmoid sinus thrombosis was made. Before operation was performed the infection was combatted by the administration of 20,000 units of penicillin every three hours and, after a large initial dose, 1 gram of sulfadiazine every four hours. However, six days of this therapy did not alter the course of the disease.

On September 6, endaural radical mastoidectomy was performed (fig. 1). A large perisinus abscess and an abscess within the sigmoid sinus were found. The distal and proximal ends of the sigmoid sinus were thrombosed. Contrary to the standard accepted methods of treatment only the sinus and perisinus abscesses were drained and the thrombus of the distal and proximal ends was not disturbed.

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H.C., Colored male 22 years of age

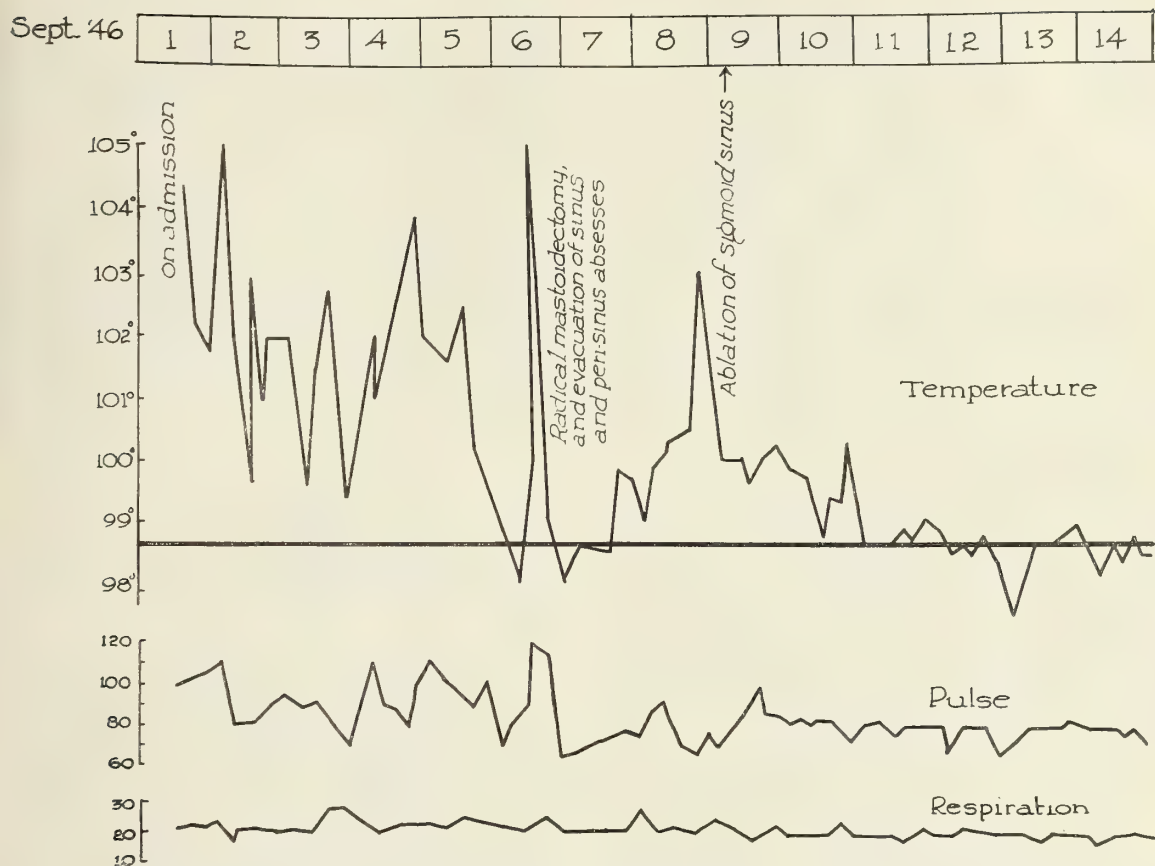


Fig. 1 is the graphic temperature chart of this case of sigmoid sinus thrombosis caused by a gram-negative bacillus. There was no response to five days of intensive sulfadiazine and penicillin therapy. Surgical drainage on the sixth hospital day produced temporary remission. However, the temperature did not subside until the septic thrombus was removed from the sinus.

Culture of the abscess revealed a gram-negative rod, which was not viable on sub-culture and could not be identified. In all probability it was *Bacillus proteus*. In any case, it was clinically resistant to chemotherapy.

The temperature remained normal for nearly 24 hours following evacuation of the abscessed cavity. Within 48 hours postoperatively the patient's temperature was 100.4 F. and before the patient reached the operating room the next morning, it had risen to 103 F.

On September 9, 1946, the mastoid was reopened through a classical postauricular incision with an accessory perpendicular incision extending backward over the transverse sinus (fig. 1). Through this incision the perisinus abscess was widely exposed until healthy dura was obtained on the medial and posterior aspects of the perisinus abscess. To obtain bleeding from the upper end of the sigmoid sinus it was necessary to expose and open the anterior third of the transverse sinus and evacuate the septic thrombus with a catheter placed on the end of the suction tube. Free and

copious bleeding was obtained from the distal end of the sinus and the sinus was allowed to bleed sufficiently to wash away all septic clots. No bleeding was obtained from the proximal end of the sinus although the catheter was inserted through the jugular bulb into the upper end of the jugular vein. The wound was packed with iodoform gauze and the postauricular incisions were closed. Twenty-four hours later, at the end of the tenth hospital day the patient's temperature reached normal and remained thus for the month during which the patient was in the hospital for dressings and postoperative care.

The patient continued to receive penicillin and sulfadiazine for five days after the temperature became normal—a total of sixteen continuous days of sulfadiazine and penicillin therapy. During this period the average daily fluid intake was charted as 4,000 c.c., the average daily urine output was charted as 3,250 c.c. In the presence of the gram-negative rod it is questionable whether chemotherapy in any way altered the course of this infection.

From the time of ablation of the sigmoid sinus, the patient's postoperative course was entirely uneventful. Five days after ablation the packs were changed under general anesthesia and at regular intervals thereafter without the use of general anesthesia. To facilitate healing of the radical mastoid cavity a split-thickness skin graft, taken from the left leg was placed over the roof and medial walls on October 3, 1946. No graft was placed over the still infected region. Where it was applied, the skin graft took 100 per cent. At the patient's request he was discharged from the hospital on October 10, 1946.

He returned to his home where his physician reports that his convalescence continued uneventfully and that the radical mastoid cavity is now completely dry.

Sigmoid sinus thrombosis has become a medical curiosity since the advent of the sulfonamides and penicillin. When it does occur, it no longer presents the classical symptomatology and findings and is not accompanied by the previously high mortality rate. With adequate chemotherapy the otologist may in time be taught to treat sigmoid sinus thrombosis medically or with more conservative surgical procedures.

#### DISCUSSION

Sulfonamides and penicillin are effective in two different ways. First, they control infections of the middle ear and mastoid, consequently greatly reducing the incidence of mastoiditis and its complications. Secondly, these drugs have an inhibiting effect on the surgeon. Mastoid infections are no longer regarded as emergencies. The eager surgeon no longer operates immediately on acute mastoiditis, thus spreading the infection in all directions. These drugs have given the otologist equanimity.

Chills, spiking temperature, high white blood count and a positive blood culture in the presence of an acute or chronic infection of the ear were formerly the characteristic findings in sigmoid sinus thrombosis. Rarely does one now have the opportunity to take a blood culture before the patient has received some drug which makes the blood culture negative and the white cell count normal. These drugs often completely mask the infection so that classical findings of sigmoid sinus thrombosis do not occur until the therapeutic measures have been dis-

continued; or, as in this case, the infection may be drug resistant and the fever will persist in spite of adequate therapy. These drugs have reduced the mortality rate of sigmoid sinus thrombosis from 30 to 40 per cent to around 5 per cent.

It may arouse debate to state that early sigmoid sinus thrombosis may in some cases be treated medically. All of you have seen patients with fulminating acute suppurative otitis media in whom all the classical signs of sigmoid sinus thrombosis developed early in the course of the acute infection. Such patients probably present periphringitis with a mural thrombus sending emboli into the blood stream. In the absence of destructive or necrotizing disease I am certain that many such infections have been and will continue to be cured by drugs alone.

With the chemotherapeutic measures acting as a barrier to the spread of infection it may be that in the future we will learn that established surgical rules may be modified and that sigmoid sinus thrombosis will respond to more conservative measures. Recently, a personal communication from Verling Hart of North Carolina told of a case of sigmoid sinus thrombosis which he cured by simply evacuating the abscess within the sigmoid sinus, no effort having been made to obtain free bleeding from the distal or proximal end of the sinus. In the case reported here this more conservative measure was courageously tried at the first operation without avail. The infection did not respond until the sigmoid and transverse sinuses were opened and free bleeding was obtained from the transverse sinus. It was, however, unnecessary to ligate the internal jugular vein. But, jugular ligation is of proved value when the infection has not responded to simple ablation of the sigmoid sinus. Nevertheless, there will always be cases of sigmoid sinus thrombosis which must be treated surgically because of drug resistant organisms and the necessity for drainage of abscess cavities.

Gerzog<sup>1</sup> and Dearmin and Sims<sup>2</sup> have reported cases of thrombosis of a lateral sinus caused by the *Bacillus proteus*. They make



the following points relative to the otogenic behavior of *Bacillus proteus*. First, the site of infection is usually a chronic discharging ear, the bacillus acting as a secondary invader in most instances. Secondly, the vascularity of the field appears extremely inviting to the organism with the result that perisinus abscesses and lateral sinus thromboses are frequent. Finally, the progression in these cases is woefully extensive, meningitis and abscess of the brain often resulting.

#### CONCLUSIONS

When sigmoid sinus thrombosis is suspected, we have adopted the following arbitrary rules: (1) An attempt is made to obtain blood cultures and blood counts before instituting any chemotherapeutic measure. (2) The infection is given an adequate trial on a course of combined sulfonamide and penicillin therapy with all supportive measures (if possible at least three days). (3) If sigmoid sinus operation is indicated, any perisinus abscess should be widely exposed until normal dura has been obtained in all directions. The sigmoid sinus is then opened and an attempt is made to obtain free bleeding from both extremities if necessary, going posteriorly to the torcula to obtain free bleeding from the transverse sinus. (4) Ligation of the internal jugular is reserved for those cases which do not respond to ablation of the sigmoid sinus. (5) The patient is given adequate sulfonamide and penicillin therapy until the temperature is normal for at least five days.

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## FACIAL NERVE PARALYSIS RESULTING FROM FRACTURE OF THE TEMPORAL BONE\*

### REPORT OF A CASE

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NEW ORLEANS

Facial paralysis, the most grotesque complication of disease of the temporal bone, most often results from a fracture of the temporal bone, Bell's palsy, acute or chronic otitis media and mastoiditis or operative injury. Ballance and Duel<sup>1</sup> have stated that the time to operate upon facial paralysis is now, "now" being the earliest possible time that the patient can be prepared for operation. This opinion is subject to debate among otologists. The following case is presented to introduce the subject of facial paralysis and to clarify the indications for surgical intervention.

#### CASE REPORT

R. B., a 22 year old negro man, was admitted to Charity Hospital in New Orleans on August 9, 1946, complaining of a profuse, purulent discharge from the left ear and facial paralysis on the left side.

On June 15, 1946, the patient received a severe blow behind the left ear. He was brought to Charity Hospital unconscious, there was bleeding from the left ear and the left side of his face was completely paralyzed. He remained unconscious for six days. Lumbar puncture revealed grossly bloody spinal fluid. The Kahn reaction was positive. To prevent infection the patient was given 800,000 units of penicillin. He recovered from the skull fracture and when he was permitted to leave the hospital, his only complaints were a discharging left ear and facial paralysis on the left.

Otologic examination on readmission August 9, 1946 revealed a copious purulent discharge which entered the left external auditory canal from a fistulous tract through the posterior superior bony canal wall. A probe could be inserted through this

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fistula to the region of the mastoid antrum. The fistula was surrounded by spicules of dead bone. The drum membrane was intact and relatively normal. The patient had fair hearing in the left ear.

All the muscles of the left side of the face were completely paralyzed. Special tests revealed loss of taste on the anterior two-thirds of the left side of the tongue. Faradic stimulation of the trunk of the facial nerve produced no response. There was slight response of the obicularis oculi and quadratus labii inferioris to faradic stimulation. The response was sluggish to galvanic stimulation of all branches.

Roentgenograms revealed diffuse clouding of the left mastoid and evidence of the old fracture into the temporal bone. The blood Kahn reaction remained positive in spite of the previous administration of 800,000 units of penicillin.

On August 15, 1946, left simple mastoidectomy was performed and the vertical course of the facial nerve was decompressed. All the mastoid air cells were filled with purulent exudate. There was moderate bone destruction and excessive bleeding throughout the procedure. The fracture of the temporal bone had extended through the roof of the antrum and had involved the dura. As a result, the temporal lobe herniated into the mastoid antrum and the superior portion of the mastoid cavity. The herniation measured 1 by 1 by 2 cm. The brain hernia was retracted to complete the mastoid operation. Exploration of the infralabyrinthine area revealed a comminuted fracture immediately below the posterior semicircular canal. Decompression of the vertical course of the facial nerve disclosed several small spicules of bone impinging upon the medial and posterior surfaces of the facial nerve immediately below the horizontal semicircular canal. These spicules were removed. The underlying portion of the facial nerve was contused and edematous.

The small fistulous tract into the external auditory canal was debrided and the bony sequestra were removed. One hundred thousand units of penicillin was placed in the mastoid cavity and the upper two-thirds of the postauricular incision was closed. A Penrose drain was placed in the wound extending down to the region of the mastoid antrum. Postoperatively, meningitis developed. This responded to the administration of 3,500,000 units of penicillin intramuscularly and 160,000 units intrathecally.

At the time of this report, five months postoperatively, the patient has serviceable hearing in the dry left ear and there is partial return of function to all the muscles of the left side of the face (fig. 1). Complete recovery of this facial paralysis is anticipated.

#### DISCUSSION

We believe that decompressing the facial nerve and removing the impinging spicules of bone facilitated recovery of function of the facial nerve in this case. The indications for the simple mastoidectomy are definite; one may debate the indication for decompressing the facial nerve. Possibly, the function would have been recovered at the same speed without surgical intervention. However, to wait for spontaneous recovery would mean to wait for six months to a year for return of function without knowing the condition of the nerve which may have been either contused or partially or completely lacerated. Decompression is believed to benefit a contused nerve. In the case of a cut nerve procrastination is futile. Therefore, early exploration of any facial paralysis resulting from fracture of a temporal bone is the treatment of choice.

Surgical treatment for Bell's palsy has been subject to considerable debate. Simple Bell's palsy is believed to be of two types, peripheral and central. The peripheral type is thought to be caused by edema of the facial nerve at the stylomastoid foramen. The central or herpetic type (not to be confused with central facial paralysis) involves the geniculate ganglion and has associated disturbances of lacrimation and sweating. Surgical treatment is not advocated for the central type of Bell's palsy. Some authors recommend early decompression of the facial nerve at the stylomastoid foramen in the peripheral type of Bell's palsy. We have seen few cases of Bell's palsy which did not progress to spontaneous recovery. We, therefore, do not believe surgical treatment is advisable in these cases unless the paralysis fails to recover or unless there is loss of response to faradic stimulation at the end of three months' observation. Such cases are rare.

Facial paralysis developing in acute suppurative otitis media is probably secondary to localized neuritis resulting from spread of infection through a natural dehiscence in the fallopian canal. Such facial paralyses which develop in the first two weeks of an acute attack of otitis media do not warrant



surgical intervention since they respond to the treatment for otitis media.

Facial paralysis which develops during the latter or destructive phase of acute suppurative otitis media warrants immediate surgical intervention. In acute suppurative mastoiditis simple mastoidectomy will usually suffice. In chronic suppurative mastoiditis radical mastoidectomy should be performed with removal of all the pathologic process surrounding the exposed facial nerve.

Postoperative facial paralysis appearing immediately after the patient recovers from the anesthetic should be explored promptly. Facial paralysis which develops a few days postoperatively will probably recover spontaneously although some surgeons advise decompression.

Operation on the facial nerve may con-

sist of a simple decompression of the nerve, of decompression and end-to-end anastomosis of a cut nerve or of nerve grafting. Decompression of the facial nerve at the stylo-mastoid foramen is advocated for the peripheral type of Bell's palsy. Decompression of the injured portion of the facial nerve is advisable in temporal bone fractures. Decompression and end-to-end anastomosis of a facial nerve may be performed if only 1 to 2 mm. of the nerve substance has been lost. Decompression and rerouting of the facial nerve in a new fallopian canal cut along the anterior wall of the external auditory canal is recommended if up to 23 mm. of nerve substance has been lost. Most surgeons, however, prefer to replace this lost nerve by a nerve graft into the fallopian canal.

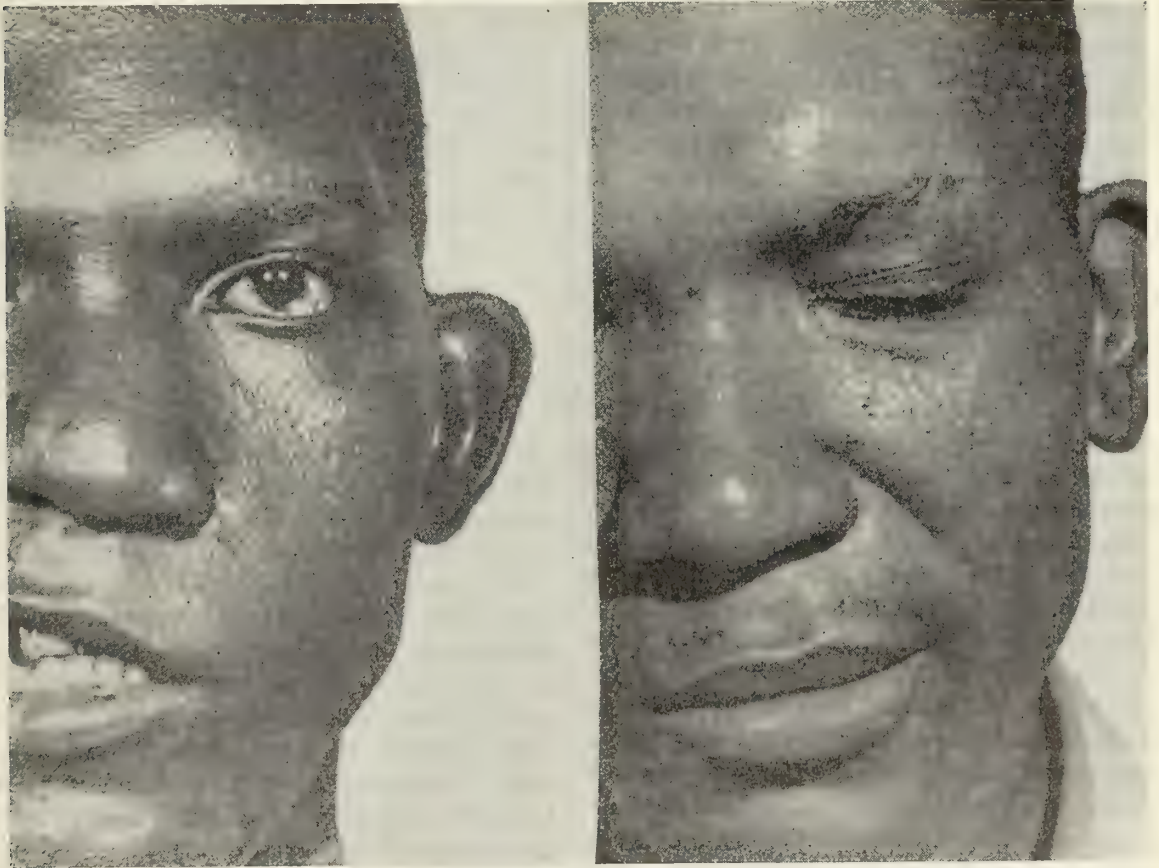


Fig. 1. The photograph on left (A) demonstrates left complete paralysis of all branches of facial nerve. The photograph on the right (B) demonstrates the return of function of all branches of facial nerve following decompression of the vertical course of the nerve and the removal of impinging bone spicules.

## COMMENT

Regardless of the method used intratemporal restoration of the continuity of the facial nerve is to be preferred to anastomosis with the glossopharyngeal or the spinal accessory nerve, as the plastic surgeon's correction of the deformity, for intratemporal operation is the only hope of restoring bilaterally coordinated emotional expression.

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## A SURVEY OF GENERAL AND OVARIAN STERILITY WITH SPECIAL REFERENCE TO ANOVULATION\*

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NEW ORLEANS

Sterility has been a problem of grave personal and social import, and one of absorbing medical interest, throughout recorded history. The plight of the sterile wife was always an unhappy one, for, tortured by her longing for a child, she was also doomed to be ostracized, abandoned, beaten, even burned alive by primitive society. Infertility was held to be a peculiar crime of females, and the reasons behind the harsh punishment meted out to the unproductive one were of a magical and an economic nature. Offspring represented wealth, for every child meant an addition to the available labor, and a bigger farm or a greater herd thereby accrued to the paterfamilias. Moreover a sterile woman was bewitched, and the contagion of her evil barrenness caused the crops to dry up, the orchards not to bear, and the cattle not to multiply, but to sicken and die. Even to recent years the Baganda of Africa authorized divorce of a childless wife for the reason that her sickness is contagious to the fruit trees and crops.

In later times, when some attempts were made to find the reasons and the treatment

for sterility, the wife had to undergo diagnostic and therapeutic ordeals scarcely less formidable than the alternatives of the savage days. The history of the ideas on origin and therapy of sterility, as outlined in Ricci's *Genealogy of Gynecology*, is fascinating to follow:

Hippocrates (460-377 B. C.) listed as causes for sterility, malpositions of the cervix, excessive smoothness of the lining of the uterus, prolapse, obstruction of the os ("the veins of the uterus becoming so large they do not retain the semen") and profuse menstruation ("the blood vessels are too weak to hold the semen").

Physicians of the Alexandrian school founded around 307 B. C. were indebted to Aristotle for many of the still valid observations he made on the physiology of fertility. He states that menstruation usually begins at 13, ceases at 40, but had been known to continue up to age 50; he bounded the reproductive epoch by these two events. Probably the first recorded idea that male sterility is worthy of consideration is embodied in his observation that women who are barren in one marriage may be fertile in another. The question of incompatibility between sperm and ovum, undecided to this day, was raised at that time.

Around 2 A. D., in the medical writings of Rome were appearing the beginnings of the recognition of endocrine syndromes associated with barrenness. If women were "not too long nor too thickset, not too fat nor too flabby, not too moist nor too dry, with cervixes not too open nor too closed, those who menstruate regularly"—these were fertile. Also "those who do not possess large and fleshy loins, and those who are mannish in their physique are sterile." One of the remedies was "lion's fat softened with rose oil", on the presumable basis of that animal's vaunted potency and maleness. The testicles of an ass, along similar lines of reasoning, were being used to cure impotency. These crude harbingers of organotherapy were but a sample of that vast and inconceivably ancient body of lore known to anthropologists as homeopathic magic—the procedure of attempting to

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\*Awarded third place in the Schering Corporation's 1946 national essay contest on "The Role of Hormones in Sterility."



bring about a phenomenon by the imitation thereof, usually assisted by powerful incantations. The same principles are applied by quacks today, and curiously enough, when intelligently applied by some of our reputable hormone theorists, are achieving some success today in the form of cyclic endocrine therapy.

Next to occupy the historical scene is Abn Ali Husayn Ibn Sina Avicenna (980-1037), the giant of Arabian medicine, and indeed, of European for five centuries. An enormous dissipator and equally prodigious writer, he turned out twenty major treatises. Chief among these is the famous *Canon*, in which appear the luminous words destined to Cassandra's fate for the next thousand years: "Sterility is due to causes involving both the male and the female." Psychic disorders were also invoked by this most discerning of savants, and diseases of the "sperm" of both partners. Some of his less illuminating comments reveal a bizarre misconception of female anatomy probably rivalled only by that of the average modern businessman, for example the procedure for the diagnosis of sterility: "The older method of fumigating the vagina with aromatics and directing the fumes into the matrix by means of a funnel (traitectario) is preferable; if the aromatic odor does not exhale from the mouth or nose there is sufficient indication that the woman is sterile."

Passing lightly over a large and much muddled and misguided era characterized by mass malpractice and religious suppression of all original publication differing seriously with Galen, we arrive at the Renaissance. Here the pendulum reached a new amplitude of magical speculation and fancy, and the original, often keenly observant methods of the ancients were largely submerged in the highly imaginative compounding of esoteric prescriptions to awe the unlettered and confound the credulous. Some of the more intelligible nostrums included rabbit saliva or mare's milk drunk immediately before coitus; Johannes de Ketham (c. 1460) considered tampons soaked in oil with the powdered right testi-

cle of a weasel to be remarkably efficacious. Sennert of Wittenburg (1572-1637), a leader of the psychosomatic trend of that day, observed that sterility was sometimes due to "imbecility of the uterus."

Around 1709 Carlo Musitano prescribed obscene entertainment for sterility, and as late as 1739 the view was publicized that if a woman stood in the right place, at the opportune time where animalculae were floating in the air, and the west wind was blowing, she became pregnant.

All was not darkness, however, in the eighteenth century's concepts of sterility. Perhaps the new dawn of the logical approach to this problem was seen in a treatise by Martin Naboth, written in 1707, and mentioning as etiologic conditions sclerotic ovaries and closed tubes. This work was written around the beginnings of the anatomic-histologic approaches to all medical questions. Morgagni gave a valuable resumé of the anatomic factors in sterility, including sclerotic ovary, absence or diseases of ovarian follicles, anomalies of vagina and external genitals, absence of uterus, obliquities of uterus, and occlusion of the tubes.

Paralleling the halting advance in the gynecologic study of infertility, the study of sex hormone physiology was highlighted by the idea of Thomas Willis (1622-1675), who suggested that puberty occurred as a result of ferments which generated in the gonads and passed into the blood stream. Bichat furnished experimental proof that the secretions of the endocrine organs were essential to vital activities by his observations of the effects of testicular and ovarian secretions on spayed animals and eunuchs. The same year, 1799, John Hunter performed the first artificial insemination of a woman. DeGraff's studies on the ovarian follicle and corpus luteum and Cruikshank's investigation of ovarian tubal migration placed reproductive physiology on a firm foundation, upon which rests much of the experimental work that has followed.

Hormonology progressed apace, with the description by Berthod of the psychosomatic effects of castration, (1849), and the

experiments of Brown-Sequard with testicular extract at the turn of the century.

During the first ten years or so of this century hormone studies consisted of experimental, largely histologic, work on animals. Following this were several years of research with crude glandular extracts, after which the biochemists began to describe the chemical nature of these products.

The first evidence of ovarian hormone action other than luteal was discovered by R. T. Frank in 1917, when he observed the effect of follicular fluid on the endometrium.

Smith and Engle, and Ascheim and Zondek, working independently, published in 1927 the first description of the gonadotropic function of the anterior pituitary. The gonadotropic activity of the serum of pregnant mares was brought to light in 1930 by Cole and Hart, and a year later the separation of anterior pituitary hormone into "Follicle Stimulating Hormone" (F. S. H.), and "Luteinizing Hormone" (L. H.) was announced by Fevold, Hisaw, and co-workers. Wassen-Lawrence published studies on F. S. H. and L. H. not long afterward. Moore and Price confirmed the findings of Smith and Engle in 1932. Demonstrating their findings by laparotomy, Davis and Koff laid the foundation of gonadotropic therapy in 1937 when they showed that ovulation in women could be induced by the intravenous administration of "Pregnant Mare's Serum" (P. M. S.).

Turning again to the subject of sterility investigation, the roster of contributors in the twentieth century is studded with famous names. To Huhner goes the credit for the post-coital test of seminal adequacy that turned the spotlight of diagnostic inquiry full upon the husband for the first time. G. L. Moench taught us most of what is known about abnormal morphology and activity of spermatozoa, while Cary and Rubin contributed tubal insufflation for the diagnosis of the biggest factor in female sterility.

Burr, Rock, Hill, Allen, Rubinstein, Zuck, and their co-workers are credited with several excellent methods of timing the day

of ovulation. Hartman's experimental work on ovulation and the clinical studies of Ogi-no and Knaus on fertile and sterile periods in relation to ovulation are classics. Novak's description of the anovulatory cycle, and Hamblen's interpretations of endometrial biopsy for its diagnosis and his cyclic gonadotropic and steroid therapy for its correction, have well begun the solution of an as yet tangled problem. Clinical studies have been remarkably facilitated by Dickinson's contributions in sexual anatomy and Meaker's crystallization of what is known of a complex subject in his masterfully conceived diagnostic schedules. To mention with praise all the outstanding workers in the field of sterility needs a tome, and to do justice to what has been accomplished in this century alone, several volumes—yet the developments in the endocrine aspects of the subjects are in embryo, and vast possibilities are still untapped for research in prevention.

The barren marriage is still a personal and social problem of pressing concern. Magnitude of the public aspects of it would appear to be increasing: There is a 200 year old downward slope in birth rate in this country, interrupted only by the spurts of increase during war times, and a steep decline over the last fifty years. Decrease in birth rate in itself constitutes no threat of depopulation in the United States, but there has been found to exist a disadvantageous scatter of fertility among the various population groups. It is clear that those least fitted by education, health, and economic advantage to have offspring have many more than those ideally prepared for reproduction. Group and racial differences in fecundity occur along geographical, social, religious, and economic lines, and most are explicable on the basis of the ability to obtain, and knowledge of, the best contraceptive measures. There is no observed hereditary fertility differential.

The reasons for the relative infertility of the upper bracket are ill health and voluntary restriction in order to meet real or artificial social and economic circumstances, the latter motive being the greatest



single factor. The professional, business, and skilled labor groups in particular marry later and delay having offspring longer than do the other groups, who seem to disregard illness as a contraindication to pregnancy, and who by reason of lack of contraception, education, or other diversion, tend to exploit their prolific propensity. Voluntary sterility, however, is germane to this discussion only in that it not infrequently becomes involuntary when prevention is practiced past the peak fertility years of the late marrying couple.

All factors considered, around 17 per cent of marriages in the United States were childless over the period 1910-1930 and around 12 per cent of all marriages are involuntarily barren.

The fact that the terms "barren marriage" and "sterile mating" are so frequently used instead of "male sterility" and "female sterility" is a credit to the men who initiated the bilateral sterility studies, and especially to Meaker, who so clearly set forth the principles of the etiology of sterility: First, in the vast majority of cases of human infertility the cause is not a single one, but the product of several factors. Depending upon the relative importance assigned by different authors to the various factors causing infertility, there are 2.23 to 4.79 abnormalities per couple.

Next, the several conditions diminishing fertility in each case are very rarely limited to one partner: only 10 per cent of the husbands and 5 per cent of the wives investigated showed no evidence of decreased fertility. Defects imposing absolute sterility were found in only 30 per cent of cases, while 70 per cent showed no single causative condition. When present, defects such as azoospermia or closed tubes, imposing absolute sterility are divided about equally between the two partners. Where the inability to reproduce is relative, the male is at fault (chiefly) in 25 to 50 per cent of barren matings. Of all demonstrable abnormalities detrimental to fertility about 70 per cent are on the distaff side, which is not to say that the wife is responsible in 70 per cent of cases.

Finally, the multiple sterility factors consist of genital disorders and those of a constitutional nature. A slight diminution of fertility from constitutional causes in one partner may so multiply a similar fault in the other that the union is unproductive, although either party is still fertile in the sense that offspring might be produced in a mating with another partner of high fertility.

Much ink and fine foolscap have been lavished upon the proper definition of sterility, but for all practical purposes it is the inability to produce living children after honest effort has been made for several years. Strictly speaking, female sterility is the inability to conceive after two or more years of marital intercourse, in the absence of prevention, with a normal man. Since the reproductive function of the ovary extends past the moment of conception, ovarian sterility is less simple to define; it may be designated as failure of conception, or of early nidatory maintenance of the fertilized ovum, by reason of deficiency or failure of the several ovarian functions.

The foundation of diagnostic methods and the rationale behind therapies directed against sterility consist of the laboriously evolved and now widely accepted ideas of generative development and reproductive physiology. It is assumed that the reader has already been exposed to all the accepted as well as the unaccepted notions on the subject—so we shall not burden him further therewith. Suffice it to say that the reader should bear constantly in mind all the steps in the developmental, anatomical, and functional history of the male and female reproductive systems, as well as all the facts he can muster on hormone physiology of same—throughout the rest of this discussion.

Throughout its development and the fulfillment of its destiny the reproductive system more than any other is constantly influenced by its own internal secretions, those of the other endocrine glands, and the fluctuations in the level of health and general metabolism. Disorders of the endocrine glands are partly or entirely at

fault in 20 to 57 per cent of cases of sterility. What the incidence is of sterility from constitutional depression is not known, but there are some figures available on the incidences of flaws arising at the many other vulnerable links in the complex chain of reproduction:

I. Male factors: It has been stated that 90 per cent of husbands of sterile matings have some impairment of fertility, and that the male is chiefly at fault in 25 to 50 per cent of such cases; there remains to break down these estimates into the separate defects themselves.

A. Testicular function: 80 per cent show some seminal impairment, severe enough in 20 per cent to impose absolute sterility.

B. Occlusion of ducts: 5 per cent of males of sterile matings.

C. Factors of unknown incidence are those of hostile secretions, ejaculative, and other coital elements. Constitutional depressions; for example, prolonged wasting diseases, seem to lower male fertility more than any other factor. H. W. Rowe cites the following incidences of contributing endocrine causes in 100 males chosen from sterile matings:

Pituitary disorder .....	35
Thyroid .....	21
Unclassified .....	2

II. Female Factors:

A. Tubal abnormalities: The largest group of causes. Incidences range from 43 to 64 per cent among sterile women; there may be absence, hypoplasia, or obstruction, the latter being most frequent.

B. Uterine abnormalities: Obstructive and infectious lesions 2 per cent; endometrial tuberculosis 5 per cent; fibroids 12 per cent.

C. Cervical factors: Cervicitis 22 to 49 per cent; poor drainage 4 to 6 per cent; malposition of cervix 4 per cent.

D. Endocrine factors other than ovarian: In 100 women of barren matings H. W. Rowe found pituitary dysfunction to be contributory in 34, and unclassified endocrine disorder in 2 per cent. It is certain that

the incidence of endocrine causes is great, but most of their effects are mediated through the pituitary or ovary.

E. Factors of unknown incidence: Coital difficulties—Here the presenting complaint is not usually that of sterility. Abdominal factors acting to prevent the ovum from entering the tube. Constitutional, infectious, metabolic, endocrine, toxic, and psychic disorders directly or indirectly depressing ovarian function in any way.

F. Ovarian factors: It is possible for the ovary to fail in any or all of four functions. These constitute the estrogenic, the gametogenic, the ovulatory, and the progestational or luteal. From 20 to 25 per cent of all female sterility is of a functional nature; beyond this little is known of the incidence of ovarian sterility with the exception of that type resulting from failure of ovulation. Opinions differ widely on these figures; it is certain that not all of the authors use the same criteria or even the same definitions of this condition; the true incidence is probably higher than reports from sterility studies would indicate, since many women come in with the complaint of irregular, prolonged, or excessive bleeding when they are afflicted with anovulatory sterility as well.

The percentage incidence of the condition varies from 13 to 54 per cent, but the consensus runs at about 15 to 35 per cent.

About 30 per cent of sterile women presenting no other abnormality have cyclic anovular menstruation, whereas only 2 per cent of normal women are thought to show this dysfunction. In the presence of regular menses up to age 40 the chances of any one cycle being anovulatory are less than one in ten. Even in the ages 40-49, about 50 per cent of the cycles are ovulatory. No significant decrease in fertility should be effected by anovulatory cycles unless they outnumber the ovulatory.

Sterility arising from ovarian failure outranks all other types in challenge and intrinsic interest, as well as in the high proportion of hypothesis inherent in most explanations of its etiologies. It is common knowledge that sterility is often associated



with severe endocrine disease, as the pituitary or adrenocortical cachexias, giantism, acromegaly, adiposogenitalism and marked hypothyroidism; and even in these conditions the real reasons behind sterility are mostly unknown. Our concern is not with the endocrine disasters, however, for few such cases appear with the primary complaint of sterility, and if they should do so many would be judged unfit for parenthood and no therapy directed against their barrenness. Most women afflicted with endocrine sterility have one of several disorders of glandular function, usually not of an obvious nature, and the underlying factors operating against the ovary in these cases are often quite obscure. With this division of the question, then, where speculation is rife, lies our interest; in its study the following general principles have gained some acceptance:

1. Proper ovarian function is dependent upon gonadotropic stimulation by the anterior pituitary and the ovary's ability to respond.

2. When response is absent or deficient to the point of sterility the condition is called primary ovarian failure, prefixed with "early" or "late" depending upon whether mature response failed to eventuate or did so and was later lost. This concept of ovarian refractiveness is based upon the very definition of a hormone as a "chemical substance produced by glandular activity, liberated into the blood stream, and transported to distant parts of the body where it is capable of exerting catalytic action, the degree of which is determined by local electrochemical conditions existing in the cells at that particular time."

3. When stimulation by the anterior pituitary is absent or deficient to the point of sterility, the condition is known as secondary ovarian failure.

4. The chief direct cause of sterility in both primary and secondary failure is absence of ovulation. In view of that fact, the major portion of the remainder of this discussion is directed toward the causes, the diagnosis, and the treatment of anovulation, as it occurs in primary and second-

ary sterility. The latter may be thought of as anovulatory sterility chiefly due to loss of function of the anterior pituitary, then, while primary ovarian failure is sterility of mostly anovular character, due to inability of the ovary to respond to the gonadotropins.

In both primary and secondary ovarian sterility, the failure may occur in any or all of the four previously mentioned activities: the gametogenic, the ovulatory, the estrogenic, and the luteal, or progestational. It is clear that estrogenic failure necessarily implies failure in the rest of ovarian activity, and that luteal deficiency is included likewise in ovulatory failure. Sterility from purely gametopathic or luteal causes is possible and does occur to a lesser extent, while either type may be caused by most of the disorders giving rise to general ovarian failure. Actually, with the exception of some local changes adversely affecting the ovary or pituitary gland, the postulated causes of all types of ovarian sterility are similar to or identical with the causes of anovulation; so they are best discussed together to avoid undue repetition. The safety of this assertion is almost guaranteed by the paucity of definite knowledge as to the exact mechanisms by which these etiologic agents operate, and the true importance and incidence of each. These etiologies fall into endocrine and extra-endocrine categories, some affecting the ovary, the pituitary, or both, either by directly effecting local anatomic or functional damage or by constitutional depression, indirectly.

A rapid review of the endocrine glands not directly associated with the reproductive apparatus will perhaps illuminate the logic behind some of the charges levelled against these organs as contributors to ovarian failure.

1. *Thyroid*: The secretory activity of the thyroid gland is largely governed by the anterior pituitary's thyrotropic secretion (which, incidentally, is believed to be identical with L.H.), and possibly by neural stimuli from the peripheral and special sense organs and the cerebral cortex, all acting through the hypothalamicopituitary

pathway. Instances supporting the latter view are the enlargement at defloration, and the onset of exophthalmic goiter shortly after an emotional crisis. Hyperthyroidism is only rarely mentioned in sterility studies; hypothyroidism, however, is regarded as a large contributor to the disorder in several ways. The systemic depression can directly alter ovarian metabolism or indirectly alter it through its effect on the pituitary. The actions of the thyroid, the deficiencies of which are most often invoked to explain adolescent ovarian failure, anovulation, luteal deficiency, and gametopathy are the calorogenic (chiefly), then the protein mobilizing action, then the glycogenolytic. Gametopathic fault is assumed, but never proved, in cases of low-grade hypothyroidism where sterility or repeated abortions occur.

2. *Adrenals*: It is thought that disordered adrenal function may bring about ovarian sterility in the following ways:

a. The constitutional impairment of water and electrolyte metabolism may depress pituitary or ovarian function, bringing on menstrual disorders, failure of estrogenic and luteal functions, or anovulation.

b. The excess circulating androgens from adrenal tumors are thought to disrupt the ovario-endometrial-pituitary reciprocities, either by direct depression of the estrogenic metabolism or by damage of gonadotropic activity. It is also believed that a gametopathic defect is imposed.

3. *Pancreas*: Just what part the pancreas plays in reproductive inter-relations is not known, but the fact that diabetes mellitus often is accompanied by retardation of adolescence, menstrual irregularity and sterility, makes probable the explanation that general constitutional depression affecting adversely the ovary and pituitary metabolisms, is the solution. Almost certainly a gametopathic factor is present, for insulin therapy of diabetic females frequently is found to raise the incidence of pregnancy without affecting the rather high rate of abortions prevalent in these women. In older cases of diabetes early

sclerosis of ovarian vessels may operate to shorten the ovary's active life.

The general governing action of the pituitary, the secretory functions of the ovary, and the reciprocal relation between them are too well known to dwell upon. It is probable that inadequacy of the anterior pituitary during the taxing period of adolescence is responsible for most endocrinopathies leading to sterility. By the time the adult patient is seen, the pituitary (if not diseased) has recovered its normal functional adequacy, leaving as residuals hypoplastic ovaries and damaged capacities in other glands.

Causes of anovulation are made up of constitutional endocrine, non-endocrine, and some local factors mechanically preventing ovulation:

I. Non-endocrine causes, acting to depress the metabolism of the ovary, the pituitary, or both, by general constitutional impairment:

A. Dietary errors: Deficiencies of protein and of vitamins B and C; excess leading to obesity.

B. Cachexia from chronic infectious or other debilitating disease.

C. Acute infections.

D. Chronic intoxications.

E. Changes in altitude and climate.

F. Anemias and blood dyscrasias.

G. Emotional crises and psychic disorders.

II. Non-endocrine local causes:

A. Ovarian: Congenital anomalies such as aplasia or intrinsic germinal inadequacy; damage by radium, x-ray, surgery, or torsion; polycystic condition caused by fibrotic tunica albuginea; fibrosis and scarring due to pelvic inflammatory disease, endometriosis, or neoplastic change; persistent corpora lutea and uterine and adnexal displacements compromising ovarian blood supply, adnexitis, and old adnexal pregnancies.

B. Pituitary: Intrinsic germinal inadequacy, damage by surgery or radiations; tumors; abscesses, and vascular accidents of an embolic, thrombotic or hemorrhagic nature.

III. Endocrine causes of anovulation:



A. The causes of primary ovarian failure:

1. Non-endocrine constitutional causes already described.
2. Local factors affecting the ovary, already listed.
3. Germinal fault or fetal disease of the ovary.
4. Incomplete puerperal recovery, in late type primary failure.
5. Disordered thyroid, pancreatic, or adrenal function, (which have been mentioned), occurring especially prepubertally.
6. Adolescent pituitary failure, with later pituitary recovery, leaving unresponsive ovaries.
7. Adrenal cell rest (virilizing) tumors of adrenal cortex and ovary, arrhenoblastoma of ovary; and granulosa and theca cell ovarian tumors leading to hyperestrogenism, menstrual irregularity and anovulation.
8. Endometriopathic factors may primarily affect the pituitary, or upset ovario-pituitary reciprocities. Patients may secrete pregnandiol and still bleed from estrogenic endometrium; may give no progesterone response to cyclic substitutional progesterone therapy, and may fail to respond to gonadotropic therapy until uterine hyperplasia and endometrial proliferation have markedly stimulated by estrogenic therapy.
9. Hyperpituitarism causing polycystic ovary, with virilizing effects of androgen imbalance.
10. The common causes of early primary ovarian failure are:

- a. Intrinsically germinal.
- b. Childhood pituitary deficiency.
- c. Childhood hypothyroidism.
- d. Inanition from inadequate diet, or cachexia from acute or chronic illness.

B. Causes of secondary ovarian failure:

1. The non-endocrine local factors affecting the pituitary.
2. Constitutional causes affecting the pituitary.
3. Intrinsic germinal or developmental fault in the pituitary usually manifested by

its failure during periods exerting great demand as at puberty or pregnancy.

4. Pancreatic, thyroid, or adrenal disorder depressing local metabolism of pituitary.

5. Endometriopathic factors, already described.

IV. Gametopathic failure: According to Moench "Defects in either one of the two germ cells lead not only to sterility but in lesser degrees to abortion, premature labors, still-births, and fetal anomalies." Besides the general causes of anovulation, most of which are capable of imposing a gametopathic failure, there are some conditions especially notable therefor: diabetes, hypothyroidism, germinal defects, radiation injury, virilizing tumors, and grades of hypopituitary function not producing anovulation.

V. Luteal failure: The secretion of progesterone may be deficient in amount or in duration ("short luteal phase"). It is caused by essentially the same factors bringing on anovulation, and is part of the latter condition when it occurs. If there is normal ovulation followed by luteal deficiency, there occurs no nidation or poor nidation and death of the ovum.

In the diagnosis of ovarian failure, we are here chiefly concerned with identifying the condition as either primary or secondary, since choice of therapy will be so determined. Consideration will be given in detail only to those features of a case that lead to a diagnosis of one or the other condition. The diagnostic schedule that should be used in every sterility investigation will uncover these causes and indicate the therapy therefor.

Before launching into an account of the minimal requirements for an inquiry into the etiology of sterility, certain principles of diagnosis should be borne in mind.

1. Meaker states "There is no worse fallacy than to accept the first discovered abnormality as the sole cause in the case under consideration, on the unjustifiable assumption that no other causative factor is present."

2. It is essential to be assured of an ade-

quate grade of male fertility before subjecting a wife to any prolonged diagnostic or therapeutic procedure. This does not imply the omission of routine history, physical examination, and laboratory work on the female until the male is cleared.

3. The complaint of sterility in itself suggests endocrine disorder, but except in obvious cases of endocrine disaster the question of such causes arises after a thorough examination of both partners has failed to reveal a structural or major constitutional disorder in either partner.

4. The purpose of the diagnostic study is not only to discover why the marriage is barren, but also whether a pregnancy is desirable from considerations of the mother's health and the possibility of producing a normal, viable child. If during an investigation it should be found that there are present inadequately treated lues in either mate, heritable and constitutional taints, advanced and severe hormonal disorder not likely to be curable, or grave renal, cardiac, or pulmonary disease in the wife, the wisest course is to inform the couple of your opinion and abandon the investigation.

In accordance with these principles it is recommended that the male be eliminated first as a source of the sterility unless some glaring reproductive fault of the female is discovered on routine physical examination. This is accomplished by establishing that the husband is normal in the following respects:

1. History and physical establish presence of potentia and libido.

2. Blood count, serology, urinalysis, basal metabolic rate determination, all within normal limits.

3. The examination of a fresh seminal specimen for volume, motility, count, and abnormal sperm forms; this is supplemented by the Huhner post-coital examination of the wife's endocervical secretions, serving to establish delivery of sperm to the cervix, and sperm motility and viability in endocervical mucus. These two tests constitute the most significant portion of the husband's examination.

Having absolved the latter of any major

defect, the investigator next undertakes the following procedures to discover whatever abnormalities are present in the wife:

1. Complete blood count, urinalysis, serology, basal metabolic rate determination. With regard to the latter it is pertinent that very low grades of hypothyroidism can depress ovarian function, and that most of the errors in technic of basal metabolic rate determination tend to raise the reading.

2. Complete physical examination, including a careful gynecologic survey of:

- A. Tubal patency, by insufflation with CO<sub>2</sub>, or oxidized oil and subsequent roentgenography; or many physicians merely use air insufflation.

- B. Patency of cervix to sperm as judged by Huhner's test; five to twenty normal, motile sperm in the cervix indicate good delivery and reception.

- C. Endometrial biopsy, best performed within six to eighteen hours after onset of menstrual flow. If an estrogenic or immature progestational endometrium is found under microscopic examination, several more cycles should be studied, with the aid of urinary pregnandiol and basal rectal temperature methods to determine whether the cycles are habitually anovulatory.

Despite all the subjective symptoms (mid-cycle uterine bleeding and/or mittelschmerz) and objective tests of the time of ovulation, there is still no way of knowing definitely whether the release of fertilizable ova occurs. Some of the methods that have been shown to be fairly reliable are the following:

- a. Basal rectal temperature records (showing a drop, then a rise, in daily determinations made throughout the cycle, occurring usually 12 to 14 days before onset of next menstrual flow).

- b. Endometrial biopsy and examination (showing secretory, progestin stage endometrium).

- c. Potential changes between symphysis and vagina.

- d. Vaginal smear and pH of vaginal secretions.

- e. Double peak of excretion of estrogen and F. S. H.



f. Increase in amount and decrease in viscosity of endocervical secretions.

4. Further endocrine studies, if primary hypoovarianism is suspected:

a. X-ray films of the sella turcica to rule out pituitary overgrowth or local damage.

b. Determination of upper and lower measurements (crown to symphysis pubis, and symphysis to sole, respectively). Measurement of height and span.

c. X-ray films of the epiphyses of the long bones to determine the state of epiphyseal closure; delayed closure seen in hypothyroidism and hypoovarianism, as well as in other conditions. This test and visualization of ossification centers are of little value in most sterility investigations.

d. Urinary levels of gonadotropic and ovarian secretions are difficult to determine and rarely practicable under ordinary conditions.

The actual diagnosis of failure of ovulation is made by the finding of proliferative or poorly secretory endometrium on biopsy at about six to 18 hours after onset of the flow, in several cycles. That this method is fallible and needs support by the complementary method of basal rectal temperature graphs is shown by these considerations:

1. Corpus luteum can form without liberation of the ovum.

2. It can fail to form after ovulation.

3. Secretion of progesterone may be too brief or insufficient in amount.

4. The endometrium may be refractory.

"A history of amenorrhea, oligomenorrhea and irregular catamenia should arouse suspicion of anovular menstruation, sufficient to be an indication for repeated endometrial biopsies in succeeding cycles."

Once the diagnosis of anovulation has been made, the rest of the management of the case depends upon the modifying diagnosis, primary or secondary ovarian failure. For diagnostic purposes the anovulation of primary ovarian failure differs from that of the secondary type in that the former is accompanied by most of the stigmata of either arrested puberty or prema-

ture senility or menopause. If it be of the early or adolescent kind the findings will be as follows:

I. Early primary ovarian failure:

A. Minimal or no sexual maturation.

1. Internal and external genitalia remain infantile; cervix is long and conical, uterine index is less than .60 (index equals half of body length minus cervix length, average value .75).

2. Breasts are about neutral stage, and other local fat pads and crines fail to appear.

3. Menarche late or absent.

B. Disorders of bone growth; span exceeds height, lower measurement greater than upper; maturation of epiphyses and ossification centers either late or absent.

C. There is absolute sterility.

D. Endometrial biopsy shows a hypoestrogenic condition; vaginal smear and pH determination reveal a poorly cornified epithelium and a pH above normal.

E. Urinary gonadotropins are normal or elevated; urinary estrogens depressed. It is thought that when the ovary fails, the checking mechanism of the anterior pituitary is gone, so that the output of F. S. H. becomes excessive. This would seem especially true of late primary failure.

II. Late primary failure: This condition is characterized by regression and loss rather than failure of maturation of sex organs. The other two signs of primary ovarian failure, amenorrhea and absolute sterility, are prominent features of these cases.

A. Onset is during the reproductive age, and mimics the climacteric.

B. Endometrial biopsy reveals a thin, atrophic lining of the uterus.

C. There is anovulation.

D. Ovaries shrunken and sclerotic.

E. Vaginal smear shows poor cornification.

F. Regression of cervix and uterus, although not to the extent of that in early primary ovarian failure.

G. Trial with gonadotropic therapy evokes no response.

H. Urinary gonadotropins are elevated, and the estrogens are depressed.

### III. Secondary ovarian failure:

A. This condition may have only sterility, or metro-menorrhagia as the chief complaint.

B. The patient is well feminized and normally developed, showing no outward evidence of endocrine disease.

C. If extra-ovarian endocrine or non-endocrine diseases exist, their symptoms will appear, for example, Addison's disease, acromegaly.

D. Basal metabolic rate is often found to be slightly depressed. (This fact may have something to do with the lamentable practice of giving thyroid for any and every endocrine complaint or menstrual disorder.)

E. Obesity of the girdle type is a frequent finding.

F. Absence of estrogens and gonadotropins in the urine (in primary pituitary failure).

G. Or there may be high estrogen titer and no gonadotropins found in the urine, or usually, some gonadotropic activity is found, but no pre-ovulatory peak of F. S. H. excretion. In general, pregnandiol studies are not reliable.

H. A tendency to small extremities with fragile bony structure.

I. Late calcification of ossification centers.

J. Sometimes a high sugar tolerance.

K. The best diagnostic criterion is the finding by biopsy of estrogenic or poor progestational endometrium at the onset of two consecutive episodes of bleeding. In general, as previously indicated, this condition consists of abnormal uterine bleeding and sterility not associated with evidences of estrogenic failure, local gynecologic pathology, or general disease or physical impairment.

Before outlining specific therapies for these several conditions it is well to consider a few guiding principles, and to point out that excessive enthusiasm for any endocrine therapy is unjustified at this stage of our knowledge. Apparent cures by any method are always subject to the criticism

that they might be spontaneous; for example, a woman may ovulate spontaneously after several anovulatory cycles. In general, the best results are obtained by physiologic therapy: the use of androgens would seem to have no logical place in the treatment of sterility of females. So-called stimulating doses of x-ray to the ovaries and pituitary, although well championed by Kaplan and others, is generally considered to lead ultimately to more profound ovarian failure.

In the use of endocrine therapy the dictum, "No endocrine gland is stimulated by products which it, itself, produces," is a warning against injudicious deluging of the reproductive system with hormone preparations. Investigating the current practice of administering thyroid preparations indiscriminately in the therapy of all sterility, Winkelstein states, "The effect of thyroid as an adjuvant or curative measure was only demonstrated where lack of thyroid was present." Before plunging into substitutional or stimulative endocrine therapy, it is the wiser course first to give adequate treatment to extra-endocrine constitutional and local disorders contributing to sterility. Again, if hypoenestrogenism or hypopituitarism coexists with disease of the thyroid, adrenal or pancreas, priority of treatment is granted to the latter three conditions. With the foregoing reservations in mind, then, the following suggestions as to therapy of primary and secondary ovarian failure are presented:

#### A. Treatment of primary ovarian failure:

With the possible exceptions of cases due to pelvic inflammatory disease, endocrine tumors of the ovary, polycystic ovary, and occasional delayed maturation or delayed recovery from puerperal depression, the ovary of primary failure does not respond to any therapy by complete functional salvage (resumption of cyclic bleeding, spontaneous recurrence of normal ovario-endometrial relations, and occurrence of pregnancy after cessation of therapy). There are two courses of therapy open, usually employed sequentially. The first of these is



a trial with the "one or two cyclic gonadotropic" treatments described by Hamblen. If there is no response to the trial, "priming" is attempted, using estrogen and progesterone in cyclic fashion, alternating with courses of gonadotropins. Here the rationale is the possibility of an endometriopathic condition, which may allow the ovary to regain its responsive power once the disordered ovario-endometrial system is righted. Finally, if it is evident that salvage will not be obtained, substitutional therapy is undertaken for the cosmetic and psychic benefits to be derived.

The dosages used are:

1. Gonadotropic trial: Day five through day 14 give daily intramuscular injections of 400 U of P. M. S., having first tested for sensitivity to serum. Day 15 through day 24 give daily intramuscular injections of 500 IU of chorionic gonadotropins (containing L.H.). If there is bleeding during the treatments the injections are stopped; a biopsy is then performed within 12-18 hours; a progestational endometrium indicates a specific response.

2. Priming doses: Estrone sulfate, 3.75 mg. per day orally, day five through day 25; and progesterone, 10 mg. intramuscularly daily from day 15 through day 25. This is continued until the occurrence of regular menstruation and a significant degree of uterine hyperplasia is obtained; then the trial of gonadotropic cyclic dosage is used as in "1" above.

3. When these fail, as they usually will, replacement therapy is instituted. This may close the epiphyses and accomplish some secondary sex character maturation, to the patient's considerable satisfaction. If some uterine growth is thus achieved, the response of the ovary to gonadotropins may still change; the dosages are the same as those used for priming.

B. Treatment of secondary ovarian failure:

As far as conception is concerned this is the most hopeful type. Ovulation is accomplished, when successful, by the use of the "one or two cyclic gonadotropic" schedule,

with the same dosage as above. The restoration of ovulation and luteal function is rarely more than temporary; the treatment is onerous and expensive. For these reasons gonadotropic therapy is usually limited to attempts at pregnancy. It is not given for more than two cycles consecutively, allowing for two or three months rest periods between treatment series to avoid the production of antibodies to the foreign protein in the P. M. S.; for the latter reason also the patient is skin-tested for sensitivity before each series.

If the fault is endometriopathic, the patient is maintained on estrogen and progesterone substitution dosage, and occasional gonadotropic trials at pregnancy are employed as previously described. Actually, the use of any such dosage figures as have here been recommended is a stab in the dark, for every patient has different requirements. This therapy should be discontinued as soon as it becomes apparent that no response is forthcoming, remembering that glands can be depressed by the administration of their own secretions. It is claimed by Hamblen that 51 per cent of young women with this type of anovulatory failure yielded specific, although temporary, responses to the gonadotropic therapy described. If there is no response it is recommended that a cycle be skipped and therapy started in the next cycle using 1000 I U of the gonadotropes as a daily dosage. Should such strong measures "force" a pregnancy, there is found a marked tendency to early abortion, which must be circumvented by adequate doses of progesterone (10 mg. three times a week) until past the point of viability of the fetus. Some authors prescribe the simultaneous use of 10,000 rat units per day of estradiol benzoate, three times weekly.

In a review of five years' results with gonadotropic therapy, Hamblen and Davis report achievement of pregnancies in 20.3 per cent of their patients suffering from ovarian sterility.

Sterility resulting from early or late primary ovarian failure has a very poor outlook for salvage, but it is in these condi-

tions that prophylaxis can play a great part. Much of the early type is preventable by proper attention to the menstrual behavior and endocrine and constitutional status of the girl, since a slight deficiency later becoming a major threat to fertility can often be easily managed during adolescence. Other measures helpful in avoiding late primary failure are the teaching of intelligent sex hygiene, control of venereal disease, premarital advice, including practical instruction in contraceptive methods, and the avoidance of all unnecessary pelvic operations. Although there is a great deal of value in attention to such factors, by far the most arresting possibilities are in the endocrine aspects of sterility.

For several centuries this absorbing quest into the nature and manner of action of the hormones involved in fertility has

made its halting way by dint of the thousands of small but important contributions of individual workers in the basic sciences, clinical medicine, gynecology and endocrine chemistry; laborious extractions of secretions from animal sources gives way little by little to laboratory syntheses of potent imitations of the original product. During the last 25 years the progress has been tremendous, but the frontier for research in endocrinology shows no signs of disappearing; it recedes and broadens with every new discovery.

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Space would not permit the publishing of over 150 references to this article; any one interested in consulting the bibliography may obtain it from the office of the journal.

I wish to express my gratitude to Dr. B. B. Weinstein for his invaluable aid in selection of literature and suggestions for the plan of this paper.



## NEW ORLEANS

## Medical and Surgical Journal

*Established 1844*

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## THE AMERICAN MEDICAL ASSOCIATION MEETING IN ATLANTIC CITY

It is said that the recent meeting of the A. M. A. held the first part of June was the largest that has ever been held by the organization. The final figures were unobtainable when we left this seashore city but the list of registrants was still behind

time in the publication of the Association's daily bulletin. The convention in many ways was comparable to a three ring circus. There was the enormous crowd, there were innumerable activities and everybody seemed to be thrilled and excited about the whole thing.

The opening two days proved very profitable and were well liked by the attendants. There were hour or less talks delivered by prominent doctors both from this country and from abroad. The list of distinguished guests from other nations was quite impressive.

The scientific assembly as per usual was extremely well attended and always there seemed to be large crowds about the more important exhibits. The scientific assembly is well worth a trip to any meeting of the A. M. A. Nowhere that I know of is there such a concentrated mass of scientific material made readily interpretable and with the exhibitors prepared to answer questions or to make clear any detail that might not be entirely lucid.

A word must be said about the commercial exhibits. It is the commercial exhibits that help to meet the enormous expenses that necessarily occur with this meeting. These exhibits are well worth while. The physician can browse amongst the newest books of medical publishers throughout the country; he can learn about the latest in drug therapy; he can see the remarkable scientific advances made by some of the pharmaceutical houses and food manufacturers; and he can view the very latest in the field of surgical instruments.

The regular section meetings held the latter part of the week were also remarkably well attended. The enormous lecture hall in the largest auditorium in the United States which was occupied by the Section on Medicine was filled with each meeting. Another very popular feature was the panel discussion of certain aspects of diseases, their cure and their management in general. They were just about as popular as any one feature of the meeting.

All in all it well repays a man to attend the annual session of the A. M. A. This be-

ing the centennial year probably there were a few more attendants than there might otherwise have been but nevertheless the session undoubtedly would have been very large. Meetings are getting so big that there are only one or two cities that can hold them conveniently. Next year the annual meeting will be held in Chicago, the following year the organization will return to Atlantic City and the succeeding year it will be on the Pacific Coast, either San Francisco or Los Angeles whose citizens are promising to build a large auditorium.

#### A. M. A. HONORS LOUISIANIANS

The far South and the State of Louisiana have reason to feel proud of two of its medical profession. Both of these doctors have lived all their lives, until they completed their medical course, not far from the banks of the Mississippi and they have both of them the traditions of the Creoles. It just so happens that the proof of the first statement lies in the fact that the two highest honors for scientific work exhibited at the A. M. A. meeting were given to Dr. George E. Burch who received the Gold Medal and Dr. Guy Faget to whom was awarded the Silver Medal, the second prize. Dr. Burch is the son of a well known country doctor who for many years practiced at Edgard, Louisiana. Burch is a typical local product, in fact up until the time he graduated or shortly thereafter he had never been out of the State of Louisiana. The second award was given to Dr. Faget, another member of a family that has been well known in medicine for many years. Dr. Faget, in collaboration with Dr. Erickson, had a perfectly beautiful exhibit of the effect of the sulfones in the treatment of the leprous patient. Dr. Faget's family is steeped in medical tradition. One of his grandfathers was a doctor, as was an uncle. He was one of three boys who entered Tulane Medical School many years ago and graduated with excellent records. The three Doctors Faget all entered the Public Health Service, two of them are still in the service, one has resigned and is practicing in New Orleans.

We want to congratulate our two local representatives on obtaining the two highest honors in the scientific exhibit. It may not be inappropriate to add that of the four honorable mentions, one of them was given to the exhibit of Dr. Champ Lyons and his group at Tulane.

It might give pride to Tulane Alumni to know that both Burch and Faget are graduates of Tulane Medical School.

#### NEW PROFESSOR OF SURGERY AT L. S. U.

We are extremely sorry to hear of the retirement of Dr. Urban Maes as Professor of Surgery and head of the Department of Surgery at L. S. U. Dr. Maes has been appointed Professor Emeritus. We are delighted indeed with the selection of Dr. James D. Rives as Professor and head of the Department of Surgery to succeed Dr. Maes. Dr. Rives is very well known amongst our local medical profession for his surgical accomplishments. He is a man of charm and highest intelligence who has always been willing to help out a brother practitioner in distress. We look forward to a highly successful term of office for this outstanding surgeon and surgical investigator.

#### MEDICAL USE OF RADIOACTIVE ISOTOPES

In the review section of the American Journal of Medical Sciences there is an excellent article<sup>1</sup> on the medical use of radioactive isotopes in hematologic disturbances and neoplasms. It is far from the intention of the writer of this editorial to suggest that he knows very much about radioactive isotopes. An isotope refers to forms of the same element having different atomic weights. It is almost unbelievable and beyond the imagination of man that neutrons can be forced into nuclei of some atoms, producing a new atomic weight for the material and yet this particular element is chemically identical with its prototype that is not radioactive. The radioactive isotope decays with a varying degree of rapidity



and the figures are astronomical. In the instance of radiophosphorus, 35 of every million atoms are changed to stable sulfur spontaneously each minute. Some of the periods of "half life" are in seconds, others are in the terms of innumerable decades. The atom is, needless to state, extremely small but radioactivity of an isotope in terms of millicuries is again in figures almost unbelievable. A millicurie is the amount of radioactivity that has been produced by disintegration of 37 million atoms per second while one microcurie is one one-thousandth of one millicurie.

In the treatment of disease of the blood and hematopoietic system great hopes were held that this radioactive material might be of tremendous help in curing all diseases in which the bone and bone marrow are primarily affected. Unfortunately this has not been the case. The one disease that has yielded most favorably is polycythemia vera but after all this is a disease which is relatively rare and because of its rarity is of no particular significance or importance. In leukemia the results have not been particularly satisfactory. The isotope is somewhat easier to take than radiation therapy and in some respects might prove a useful adjunct to the treatment with x-ray, but on the whole the tremendous furor which was created a few years ago about this remarkable substance which would cure leukemia, Hodgkin's disease and lymphoblastoma has not eventuated, so that once again we are

placed in a position where a therapeutic agent was popularized to too great an extent by the press. Hope was held out to the sufferers of leukemia if they could just get hold of some radiophosphorus the disease would be cured. Such has not been the case to the sorrow and disappointment of innumerable sufferers.

The second very short review has to do with radio-iodine and the thyroid by F. Raymond Keating, Jr.<sup>2</sup> Here the isotope has proved of particular value in studying the normal and the abnormal thyroid gland but when radioactive iodine was first brought out it was felt that it would be possible to control without difficulty individuals who have cancer of the thyroid gland. Unfortunately this has not been substantiated after careful clinical trial. On the other hand, it is interesting to note that in a very few instances the effect has been not on the thyroid gland itself but on the distant metastases, more particularly the bony metastatic lesions. This form of treatment is certainly sufficiently suggestive to warrant a continuation of the use of radio-iodine in malignant inoperable lesions of the thyroid.

1. Hall, B. E., and Watkins, C. H.: The medical use of radioactive isotopes. I. Radioactive isotopes in hematologic disturbances and neoplasms, *Am. J. Med. Sci.*, 213:621, 1947.

2. Keating, F. Raymond, Jr.: The medical use of radioactive isotopes. II. Radio-iodine and the thyroid, *Am. J. Med. Sci.*, 213:628, 1947.

## ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

***An informed profession should be a wise one.***

### SENATE BILL 545

Immediately following the 1947 meeting of the House of Delegates of the State Society the President, Dr. Gilbert C. Anderson, appointed a special committee composed of Dr. J. P. Sanders, Chairman, and Drs. Guy R. Jones and W. P. D. Tilly, to prepare a brief on Senate Bill 545 for presentation at the hearings on this bill in

Washington. Such a brief was submitted to the Executive Committee on May 31 and after discussion of the matter as presented, the special committee with the chairman of the Congressional Committee, the first vice-president, in the absence of the president, and the secretary, revised the brief to meet the wishes of the executive Committee. This brief, in its final form, is printed in

this section of the Journal so that all members of the Society may be familiar with the stand the organization has taken in reference to this legislation. It is felt that the special committee presented the bill in an excellent manner to the Committee on Labor and Public Welfare, before whom the hearings were held, and comment carried in the bulletin from the Council on Medical Service of the American Medical Association concerning this appearance will be found immediately following copy of the brief.

BRIEF BY THE LOUISIANA STATE MEDICAL SOCIETY BEFORE THE COMMITTEE  
ON LABOR AND PUBLIC WELFARE  
UNITED STATES SENATE  
HEARINGS ON S. 545

NATIONAL HEALTH BILL

Submitted by

DR. GUY R. JONES

DR. W. P. D. TILLY

DR. J. P. SANDERS

June 6, 1947

OUR STAND TOWARD THE PRESENT  
LEGISLATION, S. 545

Senate Bill 545 concentrates all the health activities of the Federal Government under one head. We believe that this is an important change because it co-ordinates all the activities and prevents duplication of efforts. It will produce economy in the long run and will be responsible for the activities in one department. We believe that health is so important that the *Administrator should be on a cabinet level*. We thoroughly agree that the Administrator should be a native born citizen of the United States, who is a practitioner of allopathic medicine, with an experience of at least five years practice in a rural community or town of five thousand or less. We believe that a general practitioner gets closer to his patients than the specialist and, consequently, would have a greater understanding of the needs of the people. We believe that the Surgeon General of the Public Health Service, the Directors of the Medical and Hospital Care Services, Maternal and Child Welfare Services should also be similarly qualified. We strongly recommend that the medical care service be kept in the hands of the local communities to be served. The communities, including their doctors, know the communities' needs. Many of them are working on these needs and with a little help, properly placed, can solve their own problems better than they can be solved by anyone else in the world. In the event of disagreement between the local community and state agency, appeal can be made by the community to the Administrator.

LOUISIANA'S CONTRIBUTION TO  
MEDICAL CARE

This brief on Senate Bill 545, the National Health Bill, is presented for the Louisiana State Medical Society, representing a total membership of 1,659 doctors out of a total of 2,507 registered in the State of Louisiana. We are responsible for the medical care of the people of the State of Louisiana which has a population of around two and one-half million people.

Louisiana has contributed to a large extent to the present status of the high standard of medical practice in the United States. It is the home of two great medical schools, Tulane University Medical School and Louisiana State University Medical School. These two schools have trained some of the great medical men of our time. Louisiana has a total of 167 hospitals, both general and special, with a bed capacity of 9,227.

Our State Medical Society was organized sixty-seven years ago and has constantly stood for the highest type of medical practice. Through its medical schools, hospitals, medical conventions and societies, Louisiana has tried to train its doctors on the highest plane possible. Through these same organizations we have tried to keep our skirts clear of many of the isms that have crept into other states. As time has progressed we have tried to improve accordingly. We have cooperated with the Government and many other lay groups in keeping the practice of medicine free. We believe that patients get better treatment under the American plan of the present doctor-patient relationship than under any other system in the world. We are willing to vary that plan by the trial and error method whenever it seems feasible to do so.

LOUISIANA IS ATTEMPTING TO GIVE GOOD  
MEDICAL CARE TO ALL ITS PEOPLE

Economically people fall in three general classes so far as medical care is concerned:

1. The well-to-do or rich.
2. The marginal group.
3. The indigent.

The first group of people, the well-to-do or rich, are financially able to take care of themselves and, therefore, need no help or guidance.

The third group, the indigent, is very well taken care of in Louisiana through our system of Charity Hospitals, Charity Clinics, Department of Public Welfare and many other social agencies. Louisiana has seven Charity Hospitals with a bed capacity of 4,808 for care of indigent alone. There are additional beds for indigents in private hospitals throughout the state. These Charity Hospitals are strategically situated in different portions of the state. They are in close enough proximity that most any indigent person can be carried there in a short period of time. These hospitals are well equipped with x-ray, clinical and pathological laboratories, physiotherapy department, nursing



schools, graduate nurses and technicians and a well trained medical staff that can take care of any of their medical needs.

The second group, the marginal group, is the one about which we are greatly concerned. We must remember that many of our great leaders have come and are coming from this marginal group. In our eagerness to help them solve their problems we should not deprive them of the initiative that may later make them leaders in industry, the professions, or in politics. We must give such help in such a way that it will stimulate their initiatives but will not hamper their progress. The marginal group to a large extent covers four classes of people:

1. Most all farmers, particularly the small operators.
2. Large families who have moderate incomes.
3. Small families with moderate incomes who have unusual responsibility for some reason or other.
4. Those with definite low incomes because of their own inefficiency or otherwise.

Most individuals in this group are very independent. They want the better things of life but they want to pay for them. They detest charity. The farmers in particular are the most independent people in the world and that largely is the reason they are farmers even in spite of their low income. The farmers are developing cooperatives, both producers and consumers, in order to help themselves. These include medical services in many instances. Hospitalization insurance, particularly the Blue Cross plan, is well developed in Louisiana. The low income groups are particularly interested in this type of insurance to take care of those catastrophic illnesses which all too often ruin the marginal family.

The Louisiana State Medical Society has been working on a prepayment medical service for three years and was able to start issuing policies in November, 1946. The Louisiana Physicians Service is the insurance company organized and operated by the Louisiana State Medical Society. To date (seven months) over 15,000 policies have been sold in groups alone. The policy is planned to take care of catastrophic illnesses such as surgery, obstetrics and certain types of laboratory and x-ray examinations. Later we hope to take care of all the medical care of policy holders. Over seventy-five per cent of all the doctors in Louisiana have already agreed to take care of the marginal group for the nominal fee provided in this policy. The people are cooperating in this prepayment medical plan. It is the American way of solving an American problem.

The Louisiana State Medical Society has a very active Committee on Rural Medical Service. It is composed of five physicians located in different portions of the state. At our state convention held

in New Orleans four weeks ago this committee was given broad powers to cooperate with the Farm Bureau, Rural Hospital Service and other interested groups to improve rural medical care in the State of Louisiana. We are encouraging general practitioners to settle in rural areas. We are working with the State Hospital Council in locating rural hospitals at strategic areas in the rural communities as provided for under the Hill-Burton Bill. The Rural Health Committee of Louisiana is anxious to see rural people obtain just as adequate medical care as the people of urban areas.

#### MEDICAL CARE IS EXPENSIVE

The cost of good medical care has become expensive not because the doctors want it but because the patient demands it. The patient is not satisfied to go into a doctor's office for him to take his blood pressure, temperature, look at his throat, listen to his heart and write one or two prescriptions and let him go. The average patient would say that this is poor medical care. The average patient who now goes to a doctor for a complete checkup requires:

1. A complete medical history.
2. A complete physical examination.
3. Laboratory examinations whenever necessary of the blood, urine, stool, secretions of the body, blood chemistry and many special examinations that may be required.
4. An x-ray examination of any or all parts of the body that might be involved.
5. Heart tracings are frequently demanded by patients who have high blood pressure or heart disease.
6. Special eye, ear, nose, throat, kidney, stomach, rectal and other examinations may be required.

All of this means that the patient has increased the expense of his examination enormously from that which was required fifty years ago. First of all, the physician has to have a well equipped x-ray and clinical laboratory with trained technicians and nurses to operate them. More space is required and more clerical help is necessary. The treatment of the patient's condition may not be so expensive after he has been diagnosed. However, many cases may require infusions, transfusions, plasma and other expensive drugs not formerly known such as penicillin, streptomycin, et cetera. We might as well try to get our patients to go back to the horse and buggy days for their transportation as to take them back for cheap medical care. The horse and buggy cost approximately \$200.00, the old Model T could be bought for around \$600.00 while the present automobile will cost around \$1,500.00. People in the marginal group, however, require an automobile in which to ride in spite of the cost and also they want modern medical care regardless of the increased cost. None are willing to go back to the horse and buggy days.

Medical practice in this Country has progressed to the present high standard under the American plan. Whenever any attempt is made to regiment medical practice it deteriorates.

#### RECOMMENDATIONS

1. That the Administrator should be a native born citizen of the United States, who is a practitioner of allopathic medicine with an experience of at least five years practice in a rural community or town of five thousand or less.
2. That the qualifications for the Surgeon General of the Public Health Service, the Directors of the Medical and Hospital Care Services, Maternal and Child Welfare should be the same as those of the Administrator.
3. That any appropriation under this bill be a grant-in-aid on a community level.

#### CONCLUSION

We recognize Senate Bill 545, with alterations as suggested in this brief, to be the most favorable bill presently offered for the American people and the medical profession.

Excerpt from Bulletin No. 8 of the Council on

#### Medical Service on the American Medical Association

"There came from the Louisiana State Medical Society Doctors Guy R. Jones, W. P. D. Tilly and J. P. Sanders, who stated that in their opinion this bill was the best bill presented in recent years, both to the public and to the medical profession.

"They offered several suggestions for changes in the Bill particularly in its administration. They suggested that the administrator of the Act and the Directors of the different departments should be practicing physicians and experienced in general practice. They stated that the general practitioner was closer to the people and knew their needs better than men in the specialties. They said that any grants should be on a community basis and that the Administration, both community and state, should be in the hands of laymen and doctors.

"They observed that this Bill was intended to take care of that large group of people of marginal income. It was pointed out that many leaders in all walks of life came from this group and that any assistance given them should be done in such a way that it would not hamper their initiative or retard their progress."

## TRANSACTIONS OF ORLEANS PARISH MEDICAL SOCIETY

July 14, Joint Scientific and Second Quarterly Executive Meeting, Orleans Parish Medical Society, 8 p. m.

July 17, Medical Toastmasters, Hutchinson Memorial Auditorium, 8 p. m.

July 18, Lakeshore Hospital Staff, 8 p. m.

July 23, Catholic Physicians' Guild, 8 p. m.

July 24, Clinico-pathologic Conference, Touro Infirmary, 12 noon.

DePaul Sanitarium Staff, 8 p. m.

Medical Toastmasters, Hutchinson Memorial Auditorium, 8 p. m.

July 25, New Orleans Hospital Dispensary for Women and Children Staff, 8 p. m.

Aug. 4, Board of Directors, Orleans Parish Medical Society, 8 p. m.

Aug. 7, Clinico-pathologic Conference, Touro Infirmary, 12 noon.

Executive Committee, Baptist Hospital, 8 p. m.

Medical Toastmasters, Hutchinson Memorial Auditorium, 8 p. m.

#### NEWS ITEMS

Dr. Howard Mahorner addressed the Birmingham Surgical Society in Birmingham on May 26. He spoke on the surgical significance of duodenal diverticula.

Dr. John H. Musser was recently re-elected (for

the twelfth time) president of the Child Welfare and Community Health Association.

Dr. Rudolph Matas was the principal speaker at the Paul Tulane Day Ceremonies at McAlister Auditorium, May 10.

Highlight of the program was the presentation of a plaque commemorating the occasion to Dr. Matas, one of the oldest living graduates of Tulane University.

Dr. Lucy Scott Hill and Dr. Sam Nelken were elected to membership in the American Psychiatric Association at its 103rd annual meeting in New York City recently.

#### LOUISIANA HOSPITAL ASSOCIATION

Dr. Lewis E. Jarrett was elected president of the Louisiana Hospital Association at a meeting of the Association in Lafayette, May 24.

#### CHANGES IN MEMBERSHIP ROLLS

During the month—

Two physicians were separated from military service—Dr. Philip B. Johnson and Dr. Albert P. Spaar, Jr. Dr. Johnson was removed and Dr. Spaar was transferred to intern membership.

Four physicians were dropped because of non-payment of dues. (three active—Drs. John M. Carter, J. W. Rosenthal, and Marvin C. Smith; one associate—Dr. Robert P. Vincent).



## LOUISIANA STATE MEDICAL SOCIETY NEWS

## CALENDAR

## PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

## LOUISIANA STATE UNIVERSITY

The School of Medicine, Louisiana State University, announces the following appointments:

James D. Rives, formerly clinical professor of surgery, as professor and head of the Department of Surgery. Rives succeeds Urban Maes, who has retired and has been appointed professor emeritus.

Robert L. Simmons, formerly director of the Lauderdale, Mississippi Health Unit, as associate professor of Public Health and Preventive Medicine on a full-time basis. Simmons succeeds George W. McCoy, who has reached the age of retirement and has been appointed professor emeritus.

Joseph A. Danna and Narcisse F. Thiberge have also reached the age of retirement and have been appointed clinical professors emeritus of surgery and medicine, respectively.

Sidney S. Chipman, formerly in the practice of pediatrics at Norwalk, Connecticut, and during the past year a student in the School of Public Health, Yale University, as associate professor of pediatrics on a full-time basis. Chipman will be director of the post graduate extension program in pediatrics in the State of Louisiana on a joint appointment of the State University and the State Board of Health.

Nelson K. Ordway, formerly instructor in pediatrics, Yale University, as assistant professor of pediatrics on a full-time basis.

Edwin S. Kagy, formerly associate in Tropical Medicine at the School of Medicine, Tulane University, as clinical assistant professor of medicine.

Anthony Failla, formerly resident in otolaryngology at Charity Hospital, New Orleans, as instructor in otolaryngology on a full-time basis.

Henry C. McGill, formerly intern in pathology at Vanderbilt University Hospital, as assistant in pathology.

## CHARITY HOSPITAL

A meeting of the Medical Division of Charity Hospital Visiting Staff was held on Tuesday, June 17 at 8 p. m. in the Auditorium of the Hospital. The program was as follows: Miliary Tuberculosis: Response to Streptomycin Therapy by Dr.

Philip B. Johnson; Bacterial Endocarditis: Two Cases Requiring Massive Antibiotic Therapy by Drs. Norman S. Gilbert and Carl Gulotta.

## OFFICERS OF LAKESHORE HOSPITAL

At a recent meeting of the staff of Lakeshore Hospital Dr. Earl Conway Smith was re-elected president. Other officers who were also re-elected include Dr. Robert M. Willoughby, vice-president; Dr. Alan Leslie, secretary-treasurer.

The members of the Executive Committee include Drs. Robert M. Willoughby, E. D. Matthews, L. J. O'Neal, W. P. Bradburn, Jr., Irvin Cahen, E. S. Nelson, J. S. Herring, W. C. Rivenbark and Harold Kearney.

AMERICAN MEDICAL ASSOCIATION  
MEETING

The following is a list of names of doctors from Louisiana who attended the centennial meeting of the American Medical Association in Atlantic City, June 9-13, 1947.

*Alexandria:* Dr. George Vryonis.

*Cajalville:* Dr. P. T. Erickson.

*Franklin:* Dr. D. C. Nelson.

*Lockport:* Dr. Guy R. Jones.

*New Iberia:* Dr. W. P. D. Tilly.

*New Orleans:* Drs. John Adriani, Ruth Aleman, J. W. Atkinson, C. A. Bahn, Elizabeth Bass, W. D. Beacham, O. W. Bethea, C. C. Blakeney, C. L. Blumstein, D. C. Browne, G. E. Burch, Edgar Burns, A. N. Caine, W. B. Clark, E. H. Countiss, O. P. Daly, J. S. D'Antoni, M. E. DeBailey, B. J. De Laoreal, J. P. Farrior, V. H. Fuchs, Manuel Garcia, Grace A. Goldsmith, G. M. Haik, Katherine Havard, Lucy S. Hill, J. K. Howles, Edgar Hull, G. G. Johnson, R. A. Katz, A. S. Kiblinger, E. L. King, M. Lescale, F. L. Loria, M. G. Lynch, Champ Lyons, Rudolph Matas, Urban Maes, G. G. McHardy, J. H. Musser, Evelyn B. Nix, Alton Ochsner, W. J. Otis, William Parson, R. V. Platou, P. Pizzolato, C. T. Ray, I. L. Robbins, D. A. Roman-Vega, Dennis Rosenberg, P. J. Saleeby, D. N. Silverman, W. A. Sodeman, A. J. Sullivan,

W. G. Tabb, P. T. Talbot, G. J. Taquino, B. B. Weinstein, and G. N. Weiss.

*Ponchatoula:* Dr. Glenn T. Scott, Jr.

*Rayne:* Dr. E. C. Faulk.

*Shreveport:* Drs. Bodenheimer, W. H. Brown-ing, M. D. Hargrove, D. B. Snelling, J. D. Talbot, and H. M. Trifon.

*Sterlington:* Dr. B. E. Spencer.

#### WEBSTER PARISH

The Webster Parish Medical Society met Tuesday, May 27, at 7:30 p. m. at Minden Sanitarium at Minden, Louisiana. Dr. M. W. Hunter of Monroe, Louisiana, talked on The Diagnosis and Treatment of Coronary Occlusion.

#### NEWS ITEM

Dr. Roy Carl Young of Covington, La., addressed The National Association of Private Psychiatric Hospitals on The Role of the Private Psychiatric Hospitals in the Treatment of Alcoholic Addiction, at its Annual Meeting at the Pennsylvania Hotel, New York, on May 18, 1947.

Dr. Young together with several other of our local psychiatrists, attended the meeting of the American Psychiatric Association from May 19 to May 23, 1947.

Dr. George M. Haik, Head of the department of Ophthalmology at Louisiana State University presented a paper on Intra-Ocular Foreign Bodies before the American Medical Association at its recent meeting in Atlantic City, N. J.

Dr. Rufus Alldredge, Assistant Professor of Clinical Orthopedics at Tulane, was on the program of the American Orthopedic Association at Hot Springs, Virginia.

#### THE AMERICAN CONGRESS OF PHYSICAL MEDICINE

This organization will hold its twenty-fifth annual scientific and clinical session September 2-6 inclusive, at the Hotel Radisson, Minneapolis. Scientific and clinical sessions will be given the days of September 3, 4, 5 and 6. All sessions will be open to members of the medical profession in good standing with the American Medical Association. For information concerning the convention, address the American Congress of Physical Medicine, 30 North Michigan Avenue, Chicago 2, Illinois.

#### LOUISIANA - MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

The Louisiana-Mississippi Ophthalmological and Otolaryngological Society held its annual meeting at The Buena Vista Hotel, Biloxi, Mississippi, on May 5, 1947.

Dr. George Adkins of Jackson, Mississippi, Pres-

ident of the Society, presided over the meetings. The following program was presented:

The Rhinoplastic Operation and the Restoration of Nasal Function: Dr. Samuel Fomon, New York City.

Newer Trends in the Treatment of Ocular Diseases: Dr. Peter C. Kronfeld, Chicago.

The J. Raymond Hume Memorial Address: Meniere's Disease: Dr. Henry L. Williams, Rochester, Minn.

Allergic Problems Seen by the Ophthalmologist and Otolaryngologist: Dr. Ralph Bowen, Houston, Texas.

Dr. Noel Simmons of Alexandria, Louisiana was elected President, and Dr. Edley H. Jones, of Vicksburg, Mississippi was re-elected Secretary. The 1948 Convention will be held in New Orleans, Louisiana.

#### THIRD AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY

It has already been pointed out that a magnificent program is being prepared for this important meeting, of which Dr. Fred L. Adair of Chicago is general chairman and which will be held in St. Louis September 8-12. Not only is the medical profession to be represented but a recent release has come to the journal office saying that an extensive nursing program has been planned for this Third American Congress. Women in the nursing field from all over the country are scheduled to appear on the program.

#### NEW HOSPITAL IN METAIRIE

Dr. William Kohlman Gauthier, Director of the New Orleans-Metairie Hospital Foundation announced that a 30 bed general hospital will be opened in the latter part of July at 310 Codifer Boulevard, Metairie. Modern colonial architecture in design, the building incorporates the latest facilities and development in hospital equipment, including an inter-communication system that enables the nursing staff to be in constant reach of individual patients. The hospital is so constructed that expansion can readily be made.

The building is the only one in the New Orleans Area constructed specifically as a private hospital during the past 17 years, although the population during the same period has increased from 390,000 to 650,000 people.

The staff of the hospital will be organized according to the rules and regulations of the American Medical Society and the American Hospital Association. The organization will be that of an open staff hospital and all doctors who are members of local, parish or state medical societies are invited to utilize its facilities.

Certification as an accredited hospital by the American Hospital Association has been applied for. Also application has been made to handle indigent cases in certain circumstances.



## INTERNATIONAL COLLEGE OF SURGEONS

A convocation and assembly of the International College of Surgeons, United States Chapter, will be held in Chicago September 28-30-October 1-4. The General Chairman of the meeting is Dr. Raymond W. McNealy. An excellent program will be provided for those who plan to attend this meeting.

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MAJOR GENERAL BLISS NEW  
SURGEON GENERAL

It is with pleasure that we read of the announcement of Major General Bliss being appointed the new Surgeon General of the U. S. Army Medical Corps. General Bliss is a graduate of Tufts Medical College, he entered the service in 1911 and has since that time been continuously with the Medical Corps of the Army. General Bliss has had many important assignments. He has been Chief of Surgery at the Sternberg General Hospital, Manila, at Fort Sam Houston and at William Beaumont General Hospital, El Paso, Texas. In 1943 he was made Chief of Operations; a few months later Assistant Surgeon General, in which capacity he served until June 1946, when he was made Deputy Surgeon General.

At the same time it was announced that Brigadier General George E. Armstrong assumes the duties of Deputy Surgeon General.

Former Surgeon General Kirk retired from active duty and it is understood will practice in New York City. To General Kirk should go very much more credit than apparently has been given to him for the able way in which he conducted the Surgeon General's Office and the various medical services during the period of active fighting. Every student of the Army Medical Corps will appreciate that Kirk did a magnificent job. The tremendous reduction in morbidity and mortality figures show that Kirk was willing to assume responsibilities that would permit of the medical profession in this country to go ahead and do an unsurpassably good job in taking care of the sick and wounded soldier.

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DR. LUCIEN AMARON LeDOUX

A reprint of an editorial written about Dr. Lucien A. LeDoux and which appeared in the Southern Medical Journal a few months ago has come to the office of the journal. Dr. LeDoux, as the reprint points out, has been active and busy in the affairs of organized medicine. Furthermore, he has been particularly interested in the Southern Medical Association, of which he is now president-elect. We extend to Dr. LeDoux all best wishes for a successful tenure of office.

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CARE OF THE HUNGRY

CARE is a non-profit, government-approved food package service to Austria, Belgium, Czechoslovakia, France, Finland, Greece, Hungary, Italy,

Norway, the Netherlands, Poland, Rumania, the American, British and French zones of Germany plus all of Berlin. It is composed of twenty-seven major welfare agencies concerned with sending aid to Europe. It has been termed by General Eisenhower, a "personal expression of international goodwill."

The CARE food package contains more than twenty-one pounds of meat, fats, sugar, milk, flour, chocolate, coffee and other essential foods which are practically unobtainable in Europe today. Operating through agreements with the European governments, CARE guarantees delivery of its parcels ration-free, duty-free, tax-free.

Total cost of a CARE food package is \$10. Orders are airmailed to the designated countries in Europe and delivery is made from local European warehouses. Individuals and organizations can send CARE food packages to friends and relatives in Europe. Orders may be sent to CARE headquarters, 50 Broad Street, New York 4, N. Y.

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NATIONAL FOUNDATION FOR INFANTILE  
PARALYSIS, INC.

"Again during these summer months outbreaks of poliomyelitis are making their appearance in many sections of the country. Last year 25,191 cases occurred in the nation, 382 of them within this state. No one can forecast how many cases will occur this year or how badly the communities in this area will be affected. Medical science, unfortunately, cannot as yet prevent an epidemic or even one case.

"Physicians in this area, as well as elsewhere, are aware of the multitude of problems poliomyelitis presents. Treatment of the disease is apt to be prolonged and extremely costly, requiring the services of many specialists. Too often the patient's family looks to the physician for advice and guidance far beyond the immediate problem of medical care.

"In times such as these it is helpful to physicians to know that there are others prepared to share these troublesome burdens. In addition to making possible epidemic aid, education, and scientific research, the National Foundation for Infantile Paralysis is pledged to assist financially those patients who require such help. Through their generous contributions to the March of Dimes, the American people have made this possible. Hospital bills, salaries for physical therapists and nurses, purchase of special equipment, and the many other changes which may comprise the essentials of good medical care may be paid for by the Chapters of the National Foundation when necessary. Local Chapters of the National Foundation are scattered throughout the United States. There is one in or near your own community. Your local health department can furnish you with the address of the Chapter nearest you."

THE NUMBER OF BIRTHS DURING THE  
FIRST QUARTER OF 1947

There were approximately 973,000 births registered in the United States in the first three months of 1947. This is almost 50 per cent more than the number of births registered in the first three months of 1946, and it is 29 per cent more than the number recorded the first quarter of 1943, the record year until 1946.

The death rate in the country, according to the figures of the National Office of Vital Statistics was 388,000, comparable with the first quarter of 1946.

PHYSICIANS WANTED

The office of the Journal has been informed that a physician is needed for general practice in Livingston, Louisiana. For detailed information communicate with Mr. Sartwell in that locality.

A physician is wanted by the Elizabeth Sullivan Memorial Hospital in Bogalusa. For detailed information contact Dr. E. E. Lafferty at that institution.

A physician is needed in Vacherie, Louisiana. For further information contact Mr. J. Richard Haydel, Adjutant, The American Legion, Wallace Post No. 268, Vacherie, Louisiana.

HEALTH IN NEW ORLEANS

The Bureau of the Census, Department of Commerce, reported that for the week ending May 17 there occurred in the City of New Orleans 145 deaths. Figures are not available as to racial distribution of these deaths. It might be pointed out, however that there were 25 more people dying in the city than the previous week and that the number of infant deaths from both races was 20. The following week, which terminated May 24, showed a better death record than the previous week. In this week there were 134 deaths; the number of infant deaths was seven. There are no figures available for the racial distribution of these deaths but in the previous week the figures have become available and show that 96 of the deaths were in the white portion of the population and 49 in negroes. There was a very sharp reduction in the number of deaths amongst the citizenry of New Orleans for the week which closed May 31, only 93 deaths being reported, 61 of which were white, 32 negro and five deaths occurred in children under one year of age.

There was a very sharp increase in the death rate in the city for the week which closed June 7. The increase was almost 50 per cent above that of the previous week. Of the 154 people who expired in New Orleans 100 were white and 54 were non-white. Nine of the deaths occurred in infants.

INFECTIOUS DISEASES IN LOUISIANA

The weekly morbidity report for the State of Louisiana for the week which ended May 19, the following diseases were reported in numbers greater than 10: Tuberculosis for the first time in a long while led all deaths with 69 instances reported, followed by hookworm infestation with 59, cancer with 33, measles with 23, influenza 22, unclassified pneumonia 18, malaria 17, whooping cough 16, pneumococcic pneumonia 14, septic sore throat 12, other forms of tuberculosis and chickenpox 11 each. During this period of time there was one case of poliomyelitis reported which originated in this state and one case which was contracted outside the state. The following week, which closed May 17, found cancer leading the list of reportable diseases with 53 cases. This in turn was followed by 34 cases each of measles and pulmonary tuberculosis. There were 31 cases of unclassified pneumonia, 17 of chickenpox, 13 of whooping cough and 11 of pneumococcic pneumonia. There were no cases of poliomyelitis reported this week nor were there any unusual or rare diseases. For the week which came to a close on May 24, pulmonary tuberculosis again led all other reportable diseases with 62 cases listed at the Louisiana State Department of Health. Next in order of frequency was unclassified pneumonia with 29 cases, cancer and whooping cough with 21 each and measles with 19. The only unusual disease, at least for these days and times, was a case of smallpox discovered in Sabine Parish. The last week in the month was a remarkably healthy week; there were only three diseases reported in numbers greater than 10, namely measles with 27, pulmonary tuberculosis with 19 and cancer with 18.

MONTHLY MORBIDITY FOR  
VENEREAL DISEASES  
STATE OF LOUISIANA  
Month Ending April 30, 1947

	Total This Month	Total Previous Months	Total To Date 1947
Chancroid	43	178	221
Gonorrhea	1269	3800	5069
Granuloma inguinale	19	38	57
Lymphopathia venereum	7	26	33
Syphilis	949	3040	3989

BOND-A-MONTH

The following article is published at the request of the Treasury Department, U. S. Savings Bonds Division.

"CALL ON SOME DOCTORS, SON . . ."

The apple-cheeked investment salesman, freshly weaned from college, sets forth in the world with two pieces of equipment—a brief case for that dignified look, and some sound advice from his elders.



"The old-timers in stocks and bonds slap him on the back and give him the advice they had when they were young:

"Go call on some doctors," son."

It is sound advice. Doctors, too often, are good prospects for bluesky investments. When it comes to slick trading in securities, they haven't the time to investigate. They're scientists, analysts of human ailments, artists of the operating room, travellers in the night, worriers, dreamers, thinkers and curers. But not financiers.

Diagnose an illness? Sure. But when a thousand dollars could be made or lost on a one-point change in Giltedge Preferred, they're busy; a child's appendix has ruptured.

Buy the best X-ray machine at the right price? Probably. But skillfully manipulate industrial investments to put their children through college? Or to take care of the family when the old ears are not so sharply attuned to the stethoscope, hands not so sure on the scalpel? Not very often.

A doctor is a busy man and a hopeful one—hopeful that the fees will take care of the future. True, some doctors are wealthy, or near it. To most, wealth is just something someone else enjoys. But many doctors, lulled by the crowded waiting rooms which went hand-in-hand with the war-born doctor shortage, figure they'll be pretty well set for retirement, the way fees are piling up.

Yes, the doctor needs a "bullet-proof" investment, and the United States has provided it in Savings Bonds. We all know that, but just to make it available isn't enough.

Most doctors need something more. In business matters they need a string tied around a finger. The Government is offering this to them in the new Bond-a-Month Plan. Your bank ties the string, gives it a yank every month. And all the doctor has to do is leave it there. Wilson Mizner said: "The gent who wakes up and finds himself a success hasn't been asleep." As to planning his future, once the doctor has invested in Bond-a-Month, he *can* give all his attention to his important work.

Before getting down to what the Bond-a-Month Plan can do for the non-salaried doctor, let's take a look at some of the facts in the case of the average practitioner. He's busy, more of late than ever before. His routine is hospital calls, perhaps an operation or two, office hours, house calls, office records, telephoning, more calls after dinner. Every so often a baby fails to realize the doctor has a schedule, or someone breaks a leg, or gets measles. Even the specialists work no 9-to-5 day.

The U. S. Department of Commerce has made studies of doctors' incomes, based on reports of a sample of the 129,000 men and women in private practice in 1940. The studies show that the in-

come rises slowly to a maximum in the early 50's and then starts dropping. From 35 to 54 is the real money-making period.

At 35, most doctors have begun to pay off their starting-in-business debts, have built up a small neighborhood practice and are becoming known. Their practice grows with ability. By the time they are 54, other doctors, young and vigorous, have come in with new methods, machines, theories. They make inroads into the established practice of the veteran. The older man no longer so willingly drives out into the country on sick calls. Office hours are shaved a little at the start and the end of the day. There are fewer operations.

And somehow, without the doctor's really knowing why, the bank balance doesn't hold up the way it used to.

To come as close as we can to keeping the horse in front of the cart, let's see what Bond-a-Month will do and then explain why this is the solution to the doctor's problem of saving for future security.

Bond-a-Month opens systematic saving through Government bonds to anyone with income and a checking account in a bank. Until now this was available only through Payroll Savings. It operates this way:

The depositor who wishes to buy a bond each month signs a card authorizing the bank to deduct the purchase price from his checking account. The bank issues the bonds and delivers them to the customer monthly. The periodic bank statement shows payment for the bonds.

And from the first and the only time the doctor signs his authorization card, he has nothing else to do except open the envelopes the bank sends him with the bonds inside.

What does the doctor need?

1. He needs some sort of arrangement for his financial future because, according to studies of his profession, incomes of physicians are much more responsive to change in the national income than are the incomes in other professions. If the national income drops and patients no longer can afford to call on the doctor so often or to pay him as quickly, a doctor's bankbook will feel the change.

2. In most cases, the doctor has no social security or pension to fall back on. Thus, he needs something to serve as an old-age reserve.

3. He needs simplicity—an arrangement which does not call for continual checking, manipulating, buying and selling.

4. He needs safety. He cannot afford to take the risks which must be protected by constant market vigilance, by buying and selling strategically.

A savings bond plan should be the foundation upon which the doctor builds his security. There is no safer investment in the world than Savings

Bonds. There is no riskless investment which pays such a guaranteed return.

Consider:

If you invest  
monthly under the

Bond-a-Month Plan	In five years You will have	In ten years You will have
\$ 37.50	\$ 2,319.00	\$ 4,998.00
75.00	4,638.00	9,996.00
100.00	9,276.00	19,992.00
300.00	18,552.00	39,984.00

Here, for the doctor himself, are vitamins E, F and G, thoroughly tested and always compounded with interest. These "vitamins" ease common symptoms of post-middle age such as chronic worry and doubt. They are available at a bank near you. And with millions of current users, we can make this unusual guarantee: one and a third times your money back if you *are* satisfied.

#### THEOBALD ROBERT RUDOLPH 1877 - 1947

Dr. T. R. Rudolph died June 11, 1947, at the age of 70. Dr. Rudolph was a graduate of Tulane in 1902. For many years he was connected with the State Department of Health. He was a very well liked physician and will be missed by his many friends.

#### WILLIAM WORTHING CALHOUN 1868 - 1947

Dr. W. W. Calhoun died on June 11, 1947, at the age of 79. Dr. Calhoun practiced medicine in New Orleans for many years. He was a member of the parish and state medical societies until the time of his death.

#### EPHRAIM D. FRIEDRICHS 1877 - 1947

Dr. E. D. Friedrichs, who died on June 10, 1947, had been in ill health for the past several years and was retired from the active practice of medicine. Dr. Friedrichs graduated from the Tulane University School of Medicine and was at one time head surgeon of the old New Orleans Sanitarium which later became the Presbyterian Hospital.

#### JOHN ADEN LEWIS, SR., M. D. 1885-1947

Dr. J. A. Lewis, Sr., died on June 17, 1947 at the age of 62, after a protracted illness. Dr. Lewis was for many years on the staff of the Department of Medicine of Tulane University School of Medicine, and on the staffs of Baptist and Charity Hospitals. He practiced in New Orleans for 36 years and will be missed by his many patients. Dr. Lewis was a member of the Knights Templar, the Shriners, the Parish and State Medical Societies.

#### WOMAN'S AUXILIARY OFFICERS 1947-48

President, Mrs. James W. Warren, New Orleans.  
President-Elect, Mrs. O. B. Owens, 1026 Bolton Ave., Alexandria.  
1st Vice President, Mrs. Marquis C. Wiginton, Hammond.  
2nd Vice President, Mrs. W. S. Kerlin, Shreveport.  
3rd Vice President, Mrs. J. E. Touns, Baton Rouge.  
4th Vice President, Mrs. J. Boring Montgomery, Lafayette.  
Treasurer, Mrs. Jules Myron Davidson, New Orleans.  
Recording Secretary, Mrs. A. D. Tisdale, Monroe.  
Corresponding Secretary, Mrs. Tracy T. Gately, New Orleans.  
Parliamentarian, Mrs. H. B. Gessner, New Orleans.

#### A GREETING FROM THE PRESIDENT

Through the medium of the Auxiliary page in the Journal I desire to extend a greeting to the members of the Woman's Auxiliary to the Louisiana State Medical Society. First, let me express my deep appreciation for the honor you have given me in making me your president for the next year. I accept the office in all humility, for I realize the responsibilities it carries with it and the inadequacy of my own capabilities. However, I think that willingness and determination to work can make up for many shortcomings, and these attributes I modestly claim. These, coupled with your cooperation which I earnestly solicit, can carry us a long way on the road to success.

To my immediate predecessor, Mrs. Arthur D. Long, I wish to express my deep gratitude for the assistance she has given me in preparing for the office and for the excellent condition in which she left the affairs of the organization. If our accomplishments even remotely approach hers, we shall feel that we have done well.

The members of the board chosen to work with us are all women of high caliber and I know I can depend upon their support. We pledge you to do our best to follow the fine example set us by former presidents and their boards.

MRS. JAMES W. WARREN,  
President.



## BOOK REVIEWS

*The Lung*: By William Snow Miller, M. D., Sc. D.  
2d ed. 1947. Pp. 222. Springfield, Illinois, Charles C. Thomas. Price \$7.50.

The second edition of this invaluable monograph on the anatomy of the lung, presents few changes from the first edition of 1937. However, this work was so complete and so valuable for reference, that few changes were necessary in this monument to the life work of William Snow Miller. A few illustrations have been improved and additional illustrations have been inserted in the chapters on the air spaces, lymphatics and the pleura. Some new studies have been added regarding the nerves of the visceral pleura. This book remains the classic study in English which should be in the library of everyone interested in the subject.

JULIUS LANE WILSON, M. D.

*An Integrated Practice of Medicine: A Complete General Practice of Medicine from Differential Diagnosis by Presenting Symptoms to Specific Management of the Patient*: By Harold Thomas Hyman, M. D. Philadelphia, W. B. Saunders Co. 1946 1184 illus, 305 in color, 319 differential diagnostic tables. 5v. Price \$50.00.

The one stop shop, familiar to all Americans has finally come home to medicos. We will no longer need to search out many sources to obtain the medical "vittels" so essential to our medical ingestion, digestion and absorption. And what is even more important, it is all there in the form of extracts, concentrates and little-finger sketches, all obtainable with an economy of effort and time. Each generation has its system of medicine and ours is no exception, but with this revolutionary difference. It is "integrated". In the world of books, this one stands unique. The power of the atomic bomb to destroy may be compared with older instruments of destruction in magnitude. The striking superiority of the antibiotics and sulfonamides over the older bacteriostatic and -cidal agents lends itself to comparison. But of Hyman's work we read in a letter from the publisher and I quote, His "work cannot be compared with any other existing work because nothing like it has ever been published." The many important symptoms and complaints are presented in tabular form with a list of the diseases in which they are found. The several diseases with distinguished features, clinical and laboratory, of each, are numerated and by an adjoining page reference one may frisk through the four volumes with their 4131 pages, diagnostically and therapeutically refreshed. The mastery of the opus operandi may prove time-consuming, but the editor assures us that eventually you will be able to handle this system so skillfully and systematically that in no time at all you

will know all that ordinarily takes so long to learn. You will no longer need to shop in many books and seek out the secrets of the specialists, for here, in close harmony and fully integrated you will find the most diverse subjects skillfully and symphonically arranged by the conductor-editor, Dr. Harold T. Hyman and his associates. To mention a few subjects is to call attention to the fact that this work has been conceived on a grand scale. Whether its execution has fulfilled the vision of the editor is something that remains to be proven. Only the reception by the profession will show whether this is to be a better mouse-trap or another case in which the mountain brought forth a mouse. Here you will read of physical diagnosis, physical medicine, psychosomatic medicine, prognosis, physician-patient relationship, endocrinology, minor surgery, gynecology, obstetrics, eye, ear, nose and throat, pharmacology, neuropsychiatry, office organization, the technics of specialist employment, pharmacology, dermatology with many good Kodachrome illustrations. Illustrations are profuse but all have been copied from other sources. In keeping with the desire to make the work all-embracing the author has prefaced the diseases of the various body systems with a brief description of the anatomy and physiology of the organ-systems.

The reviewer feels that the sample readings were for the most part written simply, clearly and concisely. Most of the theories concerning unsolved problems have been omitted and the authors have been refreshingly frank and honest in debunking some of the solemn and opinionated utterances of the medical authorities. Yet, one cannot escape the conclusion that much of this terse and facile writing is the crystallization of years devoted to the theory and practice of medicine, surgery and their allied specialties and it is the reviewer's belief that such bald treatment of many important subjects will go for naught in enlightening the practitioner, especially in instrumental technics and electrocardiography.

The most serious criticism of the books is that they are bound volumes and this one fact would seem to lead to the disintegration of the integrated system. At one point, the author states in discussing certain therapeutic measures, that they are the result of his personal experience and he requests his reading public to write to him concerning their disagreement. What he expects to accomplish with such data is certainly not obvious as far as this system is concerned. It is to be hoped that the author does not contemplate an annual supplementary volume.

The index volume is an integral part of the

whole and one that must prove invaluable in the proper use of the system. In this day, with the tremendous advances in the science of medicine, one marvels over the necessity for the general practitioner who may be expected to be familiar with medicine, surgery and the specialties and to be fairly familiar with all procedures, diagnostic and therapeutic. He is a most courageous individual and most deserving of our praise and admiration. Beset by many tasks and with little leisure, such a system as this, encyclopedic in content, despite its shortcomings, may yet prove a worthy addition to his armamentarium.

I. L. ROBBINS, M. D.

*Treatment of Arthritis and Rheumatism in General Practice:* By Bernard Aschner, M. D. New York City, Froben Press, 1946. Pp. 340. Price \$5.00.

This book is a review of the history of rheumatism and arthritis and obviously should be of great interest to the physician who is especially interested in historical medicine. The author takes the opportunity to criticize the present-day conception of arthritis, especially in regard to therapy. In Chapter III he gives, at great length, description of some of the older remedies which have been discarded by the modern physician in dealing with arthritis. It is his opinion that most of these old therapeutic measures are far superior to those presently in vogue.

In Chapter IV there is a very interesting compilation of various arthritic cases which the author has had the occasion to treat during his professional career. Unfortunately this compilation is not arranged in any chronologic order or in reference to the etiology or treatment of the disease. These cases are interesting only from the standpoint of therapy which he has relied upon without the use of modern therapeutic agents.

One would presume from the expressions contained in the book that the treatment of arthritis has not been progressive and that we should revert to the use of drugs and the conception of etiology based on early historical clinical facts and data.

P. T. TALBOT, M. D.

*A Primer for Diabetic Patients:* By Russel M. Wilder, M. D., Ph.D., F. A. C. P. 8th ed. reset. Philadelphia, W. B. Saunders Company, 1946. Pp. 192. Price \$1.75.

This very valuable little book should be a big help to all diabetics who are willing to study it.

That Dr. Wilder expects his patients to adhere to a prescribed regimen studiously is indicated by the questions at the end of each chapter to be answered by the patient.

The conventional arrangement is followed. Various chapters describe the clinical features of the disease, examinations of the urine for sugar and for diacetic acid, insulins and their administration, the complications of diabetes, and the method of planning a diet and actually preparing menus for daily use. These chapters are sound and offer a wealth of practical advice.

One objection may be raised. In discussing mixtures of unmodified and protamine zinc insulin, the author gives detailed instructions for varying the proportions of these two insulins on the basis of the daily fractional urinalyses. It is doubtful that the average patient should be encouraged to make such changes which require the skill of the physician.

The book is clearly printed and well illustrated by a number of photographs and sketches. It is highly recommended.

SYDNEY JACOBS, M. D.

#### PUBLICATIONS RECEIVED

Froben Press, New York: *Care of the Breast* by Else K. La Roe, M. D.

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## MEDICAL ASPECT OF 6-PROPYLTHIOURACIL\*

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NEW ORLEANS

Propylthiouracil is the most recent and by far the least toxic of the goitrogenic anti-thyroid compounds that have been used clinically for the control of hyperthyroidism. A discussion of propylthiouracil, however, should best be centered around the thiouracils in general as they all have the same physiologic action, the essential difference between the individual compounds being the degree of potency and toxicity.

The era of anti-thyroid drugs began in 1943 when Astwood<sup>1</sup> and simultaneously the MacKenzies<sup>2</sup> directed attention to the thyroid depressing effect of thiourea and certain sulfonamides; these drugs had been known to cause goiter and also depress thyroid function when fed to experimental animals. An exhaustive study of more than two hundred compounds by Astwood et al.<sup>3</sup> revealed that two types of chemical structures had anti-thyroidal activities: the more active were the thiourea derivatives—having a carbonamide grouping; the less active were substances having an aminobenzene group, such as the sulfonamides. Sulfadiazine was the most active of the latter, but as a whole they were only one-

fourth as active as the thioureas. Of the thioureas, thiouracil, thiourea and thiobarbital possessed the best activity-toxicity ratio and were investigated first.<sup>4</sup>

Thiobarbital has been found to be more toxic than thiouracil routinely but is tolerated by some who show toxicity to thiouracil.

When taken orally, thiouracil is rapidly absorbed from the stomach and upper gastrointestinal tract, about 15 per cent being destroyed there. It is distributed throughout the body fluids and tissues, the largest concentrations being found in the bone marrow, thyroid, ovaries and pituitary. Excretion in the urine begins immediately and after 48-72 hours none of the drug is present in the blood or urine.<sup>6</sup>

Practically no tissue changes occur in any of the organs except the thyroid. Here, within 48 hours an increased vascularization and hyperplasia begins, with cellular proliferation and infoldings into the acini. The production of thyroid hormone is stopped and associated with this is a rapid decrease in the thyroid's ability to hold iodine, resulting in its gradual disappearance. The colloid also disappears in one to two weeks. Concomitant with the disappearance of the colloid the basal metabolic rate begins to fall. In the experimental animal evidence of enlargement of the gland occurs in a few days with a three-fold increase in size in two weeks.<sup>1, 7</sup>

The mode of action of thiouracil is to prevent the iodine to diiodotyrosine to thyroxine synthesis within the thyroid cell;<sup>8, 9</sup> this may be due to a depression of the peri-

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oxidase or cytochrome oxidase enzyme systems.<sup>10, 11</sup> However, the actual mechanism is not clear.<sup>24</sup> It does not prevent the secretion of pre-formed thyroxine, thus explaining the lag before the basal metabolic rate falls.

After six months of therapy a tendency towards involution occurs with the gland becoming smaller.<sup>1</sup>

When thiouracil is discontinued a reversal of the histologic picture takes place with involution and re-formation of colloid and thyroid hormone. The enlargement, however, is noted long after the histologic picture is normal.

No evidence of neoplasia has been seen, but the simultaneous administration of thiouracil with acetaminoflourine, a potent carcinogen, has been found to produce invasive tumors of the thyroid when either drug alone would not do so.<sup>12</sup>

The administration of iodine with thiouracil does not abolish the effect of the latter but it does cause a certain amount of involution and decreased vascularity to take place. Previous iodine administration was earlier thought to delay the action of thiouracil; however, later investigators have found no significant delay in response if iodine had been given earlier.<sup>13</sup>

The hyperplasia induced by thiouracil is due to increased production of thyroid stimulating hormone by the anterior pituitary—which is a result of the diminished thyroid hormone production. This is substantiated by the fact that hypophysectomy or administration of thyroxine completely inhibits the action of thiouracil to cause thyroid hyperplasia.<sup>1</sup> That administered thyroxine inhibits thyroid stimulating hormone production is well known.

In Graves' disease the action of thiouracil is the same. The over-producing thyroid makes no more hormone and in two to three weeks the basal metabolic rate begins to fall, requiring approximately one day of treatment for each per cent the basal metabolic rate is elevated for it to revert to normal.<sup>15</sup> The pulse rate falls, there is a gain in weight, and the symptoms of thyrotoxicosis disappear. Evidently the already over-pro-

ducing anterior pituitary—the cause of which is unknown—is not greatly stimulated. This is borne out by the fact that in except a very few instances there is little or no enlargement of the thyroid gland nor increase in exophthalmos. Indeed, some observers report a decrease in both in the majority of the cases.<sup>14</sup>

In toxic adenoma the results are the same, only the rate of response may be slower.

The remarkable certainty and smoothness with which thiouracil abolishes all symptoms of thyrotoxicosis plus the absence of "thiouracil escape" has caused its acceptance by many authorities and, almost generally, as the best preoperative drug available. Its use substantially eliminated the postoperative crisis, the necessity of multiple stage surgery, and has greatly lowered the overall mortality.<sup>15</sup> The increased vascularity and friability of the gland which earlier caused technical difficulty in its removal has been controlled by the addition of iodine during the last three weeks of treatment.

As with most other drugs, thiouracil has several disadvantages, the main one being its toxicity. It has been found to produce fever, lymphadenopathy, urticaria, headaches, purpura, jaundice, salivary gland enlargement, hematuria, edema of the legs, joint pains, leukopenia and agranulocytosis. The majority of these are uncommon and seldom necessitate discontinuance of the drug; either reducing the dosage or stopping it for two or three days causes their disappearance. Fever or agranulocytosis constitute its only serious toxic effects and usually requires its withdrawal.

The results obtained in over 5000 patients treated with thiouracil<sup>16</sup> show that in approximately 13 per cent there is some untoward reaction, in 8 to 10 per cent the reactions forcing a permanent withdrawal. The incidence of agranulocytosis is about 2.5 per cent (with a 15 to 26 per cent mortality). The overall mortality has been about 0.5 per cent. It should be pointed out that this figure includes those persons treated before the toxic effects were well



known, and also before penicillin was generally available.

Other disadvantages are an approximately 10 per cent failure rate and its low percentage of permanently induced remissions. The figures available of people followed up to 36 months show that about 50 per cent have had no recurrence after the drug's withdrawal. As thiouracil has only been used three years it is too early accurately to determine the percentage of permanent remissions. It appears that thiouracil produces a permanent remission only in milder cases of shorter duration and with smaller thyroid glands—those that are prone to remission; the more severe cases with larger glands usually require maintenance doses.

It has also been shown that thiouracil crosses the placenta and will cause thyroid hypertrophy in the fetus.<sup>17</sup> Rats born from thiouracil treated mothers had hyperplastic thyroids at birth but were normal in size and weight.<sup>18</sup> Although the hypertrophy disappeared and no ill effects were noted, thiouracil should probably be used with caution in pregnancy.

In an attempt to find less toxic anti-thyroid drugs, other compounds related to thiouracil are being investigated. Astwood found twenty-five of two hundred and twenty compounds "as active or more active than thiouracil."<sup>3</sup> Of these, propylthiouracil was the most powerful and eleven times as strong as thiouracil in the experimental animal. It has had rather extensive clinical investigation so far and has proved to be two to three times as strong as thiouracil in man. Initial doses of 150-200 mgm. daily and 25-75 mgm. daily as a maintenance after the basal metabolic rate has returned to normal is as effective as 600 mgm. daily of thiouracil initially and 200 mgm. daily for maintenance. It has also proved to be far less toxic than thiouracil. In Astwood's first 100 cases there were no toxic reactions.<sup>21</sup> Lahey reported the use of propylthiouracil in 160 patients—60 of whom had had surgery and 100 who were "in preparation for surgery." He stated that "two have already shown marked depression of the white cell

count."<sup>19</sup> Another group discontinued the drug in one of 110 cases because "mild sore throat and a fall in leucocyte count followed repeated trials."<sup>22</sup> McGavack et al. found only one case of toxicity, a severe febrile reaction, in 75 patients.<sup>20</sup> A summary of 284 other individual cases reveals a toxicity rate of 5.9 per cent leucopenia occurred in eight cases (2.8 per cent). Propylthiouracil was discontinued in three of these and was also discontinued in another case of nausea and gastro-intestinal upset—a total of four cases in which the drug could not be used.<sup>23</sup> Although no cases of agranulocytosis were reported, Bartels has reported one non-fatal case of agranulocytosis.<sup>23</sup> Propylthiouracil has been used successfully in patients who developed severe reactions to other thiourea compounds.<sup>21, 22</sup> The failure rate has been reported as about 10 per cent, although this may prove to be high.

A comparison of these figures with those of thiouracil clearly establishes the superiority of propylthiouracil as an anti-thyroid drug.

In discussing the place of anti-thyroid drugs in the treatment of thyrotoxicosis, Williams' statement<sup>6</sup> is aptly made: "The obscurity of the primary cause makes it difficult to know what the ultimate goal in treatment should be—other than to abolish the obvious manifestations of the disease."<sup>6</sup> Certainly the ultimate cure of thyrotoxicosis lies in a different realm from either thyroid surgery or anti-thyroid drugs. However, abolishing the obvious manifestations of the disease is the only choice we have now and in that propylthiouracil has an important place.

Of the several effective methods of treatment available today, the use of an anti-thyroid drug (propylthiouracil being the one of choice) until the basal metabolic rate is normal followed by subtotal thyroidectomy seems to offer the lowest mortality and at the same time the largest percentage of permanent remissions. Although a lasting remission is desirable, the most important objections to continued thiouracil treatment alone were the never ending

(though reduced) danger of agranulocytosis with its accompanying mortality, and its resultant necessity of having to follow a patient so closely for such a long period of time, possibly a lifetime. A drug such as propylthiouracil or a future one even less toxic or not toxic at all may eliminate these objections and perhaps may make thyroid removal unnecessary in the majority of cases. More definite conclusions can be reached only after propylthiouracil (or its successor) has been more completely evaluated. Radio-active iodine will also have to be evaluated; it may prove to be superior to any of the thiourea derivatives.

It must be borne in mind that drug treatment alone will not be entirely satisfactory as long as thyroid enlargement persists. The possibility that anti-thyroid drugs may predispose to malignancy, although unlikely, must be ruled out; and the tendency for malignancy to develop in adenomatous goiter probably indicates surgical removal in all cases. Also, some people will always prefer surgery for cosmetic reasons.

#### CONCLUSION

These facts indicates that although the development of non-toxic anti-thyroid drugs may place the treatment of thyrotoxicosis largely in medical hands, as a whole the treatment will have to be individualized, a certain percentage always requiring surgery. Obviously, the anti-thyroid drugs are a boon to those with complications that contraindicate an operation but in the past have had to submit to one.

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## THIOURACIL IN TOXIC THYROID DISEASE\*

ITS PREOPERATIVE USE IN A PUBLIC HOSPITAL IN A NON-ENDEMIC AREA†  
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NEW ORLEANS

Since the introduction of thiouracil as a clinical agent in 1943, one of us (F. F. B.) has used it in private practice in the preop-

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\*Read before a meeting of the Orleans Parish Medical Society, April 14, 1947.



aration for operation of approximately 20 patients with severe hyperthyroidism. For this purpose it has proved extremely satisfactory, though there has been the usual, apparently inevitable, percentage of undesirable reactions. For such a meeting as this, however, it has seemed to us that the presentation of the experience of a single surgeon with a group of patients who were selected for the administration of the drug on rather strict indications would be less useful than the presentation of a combined experience from a large public institution such as Charity Hospital of Louisiana at New Orleans.

Thiouracil was first used at Charity Hospital February 28, 1944, and between that date and March 1, 1947, 58 patients with toxic thyroid disease were prepared for operation with it, alone or in combination with iodine. During the same period 52 patients with the same disease were operated on after preparation for surgery with iodine alone. There was one death after operation in each group.

The iodine-treated group in no sense serves as a control for the thiouracil-treated group. The distribution was substantially the same as to age and race, but there were 12 men in the thiouracil group as compared to only three in the iodine group; the possible significance of that discrepancy will be pointed out later. Generally speaking, the degree of toxicity was perhaps somewhat lower in the iodine-treated group than in the thiouracil-treated group, though in numerous individual cases it seemed equally high. There was no attempt, however, to treat patients alternately with one drug or the other. Furthermore, it was often not clear why thiouracil was withheld in the cases in which it was not used. For that matter, some of the patients in whom it was used would probably have progressed quite as well without it, while some would perhaps have done better on iodine. In view of the fact that the 58 thiouracil-treated patients were managed by 30 surgeons, 13 of whom were residents, one would scarcely expect to find any considerable degree of uniformity of usage.

No attempt will be made, therefore, to present this material from a statistical standpoint, quite aside from the fact that the number of cases as a whole and in the separate disease categories is too small to make a statistical presentation valid. On the other hand, previous studies of thyroid disease<sup>1,2</sup> have engendered a familiarity with the disease as it is managed in this institution which warrants the reporting of impressions and even the drawing of certain conclusions from the material presented herewith.

#### ANALYSIS OF DATA

*Summary of Deaths:* The single death in the thiouracil-treated group of patients occurred in a 44 year old colored woman with a diffuse toxic goiter complicated by a cardiac factor who had had toxic symptoms for six months when she was first seen. She had lost 40 pounds. The blood pressure was 270/100 and the pulse rate 142 per minute. She was jaundiced and presented pitting edema of the abdomen and extremities. The initial basal metabolic rate was plus 46. The icterus index was 29.4 and later rose to 71.2 before the jaundice disappeared. The hippuric acid test of liver function showed an excretion of 0.7 gm. of sodium benzoate in one hour.

Under treatment with diuretics, digitalis, diet, sedation, thiouracil for 44 days and Lugol's solution for nine days, the patient improved materially and the basal metabolic rate reading fell to plus 21. At the end of a two month period of hospitalization she was permitted to spend Christmas at home. When she returned, her pulse rate was 86 per minute but the basal metabolic rate had risen to plus 33 and the blood pressure was 198/99. After additional preparation with thiouracil and iodine for 13 days, subtotal thyroidectomy was performed under ethylene ether (endotracheal) anesthesia. The operation, which occupied 70 minutes, was carried out without any difficulty. The patient's pulse on the table varied from 80 to 132 per minute and was always of good volume. Breathing had been noisy, however, and 10 minutes after she was re-

turned to her bed it stopped altogether. There was no response to artificial respiration, and tracheotomy was ineffective. Necropsy was not permitted, and death was attributed to cardiac causes. The basal metabolic rate reading the day before operation had been plus 32.

The single death in the iodine-treated group of patients occurred in a 41 year old colored woman with toxic diffuse disease and was also attributed to cardiac causes. The pulse rate was decreasing and there had been a minimal gain in weight, but, as in the previous case, operation was done in the face of a rising basal metabolic rate.

For a fair presentation of the status of toxic thyroid disease at the New Orleans Charity Hospital, it is necessary to point out that during the period in which these two surgical deaths occurred, seven other deaths occurred from this disease, as follows:

A 51 year old negro woman with toxic nodular goiter died on the table, presumably of cardiac causes, during the induction of ethylene-ether anesthesia, before any surgery was undertaken. She had been prepared with iodine and had had no thiouracil. The pulse rate was decreasing but the basal metabolic rate was rising when operation was done.

A 48 year old colored woman with toxic diffuse goiter complicated with cardiac disease also died on the table under the same circumstances. She had received Lugol's solution for 24 hours and thiouracil for 33 days, and also had been treated with digitalis. At the time of operation the pulse rate had fallen from 110 to 90 and the basal metabolic rate was plus 15.

The five other patients, who died without reaching the operating room, included:

A 28 year old colored woman with toxic nodular goiter who died in thyroid crisis, possibly with a cardiac element, 17 days after admission. Her basal metabolic rate was plus 77 and she had received thiouracil for two days.

A 52 year old woman with nodular toxic goiter who died a cardiac death five days

after admission. She had received thiouracil for five days.

A 70 year old white female with toxic nodular goiter who had received thiouracil on two previous admissions, with good control of toxic symptoms. She died a cardiac death 48 hours after she had been admitted for the third time.

A 62 year old colored male with toxic diffuse goiter who had received thiouracil for eight days on a previous admission. His basal metabolic rate was plus 8. He was readmitted four months later and died in crisis within 48 hours.

A 39 year old colored male with toxic diffuse goiter who died of coronary occlusion, possibly with an element of crisis, 70 days after admission to a medical ward. He had received thiouracil for 32 days, during which time his basal metabolic rate had fallen from plus 43 to plus 21.

Another death in a patient with possible toxic thyroid disease is not regarded as due to thyroid causes but to cardiac disease complicated by embolic peripheral vascular disease. The history was somewhat suggestive of thyrotoxicosis, but it was regarded merely as an unproved possibility.

*Clinical Picture:* When the toxicity of the 58 thiouracil-treated patients is graded on an ascending scale from plus 1 to plus 4, it is found that 27 of the 47 patients with diffuse toxic goiter and five of the 11 patients with toxic nodular goiter had a toxicity of plus 3 or plus 4. Seventeen presented 3 plus toxicity and 15, 4 plus. It should be emphasized that the degree of toxicity is based on the clinical impression and on repeated observations of the pulse rate. In the absence of definite manifestations of thyrotoxicosis no reliance was placed on the initial basal metabolic rate determination.

The duration of toxic symptoms, according to the patients' histories, ranged from less than a month in eight cases to five years in three cases. In 31 cases, 26 of which were instances of diffuse toxic goiter, the duration was less than six months. In 24 of the remaining cases, 19 of which were also instances of diffuse toxic goiter, symp-



toms had been present less than two years; the single fatal case is included in the latter group. Four of the five negro males in this group, three of whom were extremely toxic, had had symptoms less than a year. Both negro males with toxic nodular goiter also were extremely toxic. One had had symptoms for three months and the other for 18 months.

*Procedure:* Sixty-eight operations were performed in the 58 thiouracil-treated cases, including: Two total thyroidectomies, both on white female patients with nodular goiter; 22 stage procedures, 18 for diffuse and four for nodular goiter; 44 subtotal operations.

One operation was done under local analgesia and the remainder under ethylene or cyclopropane anesthesia combined with ether vapor. Intubation was employed in 38 cases, usually for the deliberate purpose of training residents specializing in anesthesia; the great majority of the patients did not need it.

#### ANALYSIS OF DATA IN RESPECT TO THIOURACIL

*Administration:* The usual routine of dosage was to administer thiouracil in 0.2 gm. doses three times daily. In some instances the dosage was later reduced to 0.1 gm. Duration of treatment varied from one to 54 days in 49 patients. The other nine patients were treated respectively for 60, 69, 85, 89, 90 (2 patients), 121, 123 and 222 days. Most of the patients treated for periods of time such as this represented ineffective attempts by the medical service to control the disease by thiouracil. Eleven patients received thiouracil for 14 days or less. In three of these cases the drug had to be discontinued because of untoward reactions while in three others the response was so prompt that iodine could be substituted and operation performed without further delay. The breakdown in methods of administration was as follows:

In 11 cases (10 toxic diffuse disease, one toxic nodular) thiouracil alone was used.

In 20 cases (19 toxic diffuse disease, one toxic nodular) thiouracil and iodine were used simultaneously. The single fatal case is included in this group.

In 27 cases (18 toxic diffuse disease, nine toxic nodular) thiouracil was discontinued before iodine was begun.

It should be added here that 13 of the 58 patients had previously been treated with iodine, with good results from the standpoint of control of toxicity in two cases, fair results in six and poor results in five.

*Reactions:* In 14 of the 58 thiouracil-treated patients there were 27 reactions, distributed as follows:

Agranulocytosis and leukopenia of varying degrees in 10 patients, combined in one case with edema and arthralgia.

Edema and arthralgia in one patient.

Leukopenia in one patient.

Dermatitis in two patients.

The reactions occurred in five of the 11 patients with toxic nodular goiter and in nine of the 47 patients with diffuse toxic goiter. Eight of the affected patients were negroes (three males, five females) and six were white (two males, four females).

In five of the 14 patients who developed reactions it was possible, after an interval of withdrawal, to resume the drug and to continue it as long as was desired. In a sixth case the patient developed agranulocytosis and leukopenia a second time and thiouracil was permanently withdrawn, as it was in the remaining eight cases.

The most serious reaction observed occurred in a 49 year old colored male with toxic diffuse goiter. On admission his white blood cell count was 6,750 per cu. mm. It fell to 3,200 per cu. mm. after he had received 1.4 gm. of thiouracil over a four day period. The drug was withdrawn at once, but the white blood cell count continued to fall; on the day after withdrawal it was 2,600 per cu. mm., and 24 hours later there were no white cells at all in the blood specimen. The count returned to normal levels after several transfusions and four doses of pentnucleotide (10 c.c. each). The patient was then prepared for operation with Lugol's solution, and subtotal thyroidectomy was performed without further untoward incident. In another case, in which the fall in the white blood cell count was similar though less extreme, the drug could be re-

sumed after a period of withdrawal during which the patient was treated with penicillin.

*Vascular Changes in the Gland:* This series bears out the general observation that bleeding at operation is likely to be more annoying in diffuse than in nodular goiters and that patients prepared with thiouracil alone may present very troublesome hemorrhage. Vascularity was annoying at operation in only one of the 13 operations performed in the 11 patients with nodular toxic goiter; in this case the drug had been given for only four days when it had to be withdrawn because of the reaction. As this was 20 days before operation, thiouracil probably played no part in the vascular difficulty.

In the toxic diffuse group, of the 12 patients prepared with thiouracil alone, one patient presented 1 plus bleeding, two presented 2 plus, four presented 3 plus, and one presented 4 plus vascularity. Thirteen other patients prepared with thiouracil and iodine by various regimens presented abnormal bleeding ranging from 1 plus in three cases to 4 plus in four cases.

These figures are presumed to be correct. A surgeon who has been troubled by excessive bleeding during a thyroid operation is unlikely to omit mention of it in his operative notes.

*Response to Therapy:* Generally speaking, all 58 patients in this series showed a definite response to thiouracil. In all instances the pulse rate decreased, and in 51 instances the basal metabolic rate reading also decreased. The response in both these respects was quite as striking in thyrocardiac as in uncomplicated toxic thyroid disease. Sixteen patients with clearcut cardiac disease associated with thyrotoxicosis, which in two instances masked the thyroid disease, had been treated initially by digitalis, with fair but by no means striking or entirely satisfactory results. In every instance the response, when thiouracil was added, was prompt and striking. All of these cases proved, in fact, that thiouracil in thyrocardiac disease frequently serves

as a "medical" or "physiologic" thyroidec-tomy.

Thiouracil does not act as promptly as iodine and the evidence of a favorable action is therefore somewhat slower in appearing. In some instances in this series no results were noted until 21 days had elapsed, but in others improvement began when the drug had been given for only seven days. The first effect which the patient experiences is a sense of well-being, followed by a gain in weight, decrease in pulse rate and decrease in basal metabolic rate. From the standpoint of the physician the most notable response is the improved stability of the patient, who is translated from a tremulous, tearful, unstable state to what Means<sup>3</sup> has called a euthyroid state. In most stage operations little or no preparation was needed for the second stage.

In this series the response was somewhat more rapid in nodular toxic goiter than in the diffuse variety. In the literature which we have reviewed only Reveno<sup>4</sup> reports a similar experience.

The response of negroes, which does not seem to have been commented on previously in the literature, impressed us as being somewhat more rapid than that of the white patients. This is perhaps to be explained by the fact that most negroes find themselves in the hospital in circumstances far superior to those in which they live ordinarily. Their environment is comfortable, their food is good, it contains from 4,000 to 6,000 calories per day, and it is provided with no effort on their part. The negro response to iodine is no more notable than that of the white subject, and the impression that the response to thiouracil is more rapid than that of the white patient is advanced merely as an impression.

#### FOLLOW-UP

No information is available after their departure from the hospital on four of the 57 patients who survived operation. One of the four, a 27 year old negro woman with diffuse toxic goiter, refused to submit to second-stage lobectomy and deserted with a basal metabolic rate of plus 98. Another of the patients in this group, who also had



been submitted to lobectomy, returned to the clinic once or twice after she left the hospital, then disappeared.

The current status of the remaining 53 is as follows:

The period of observation after discharge from the hospital ranges from 16 to 849 days. Twenty-two patients have been followed for periods ranging from one to three months, 11 for periods between three and six months, four up to nine months, five up to 12 months, six up to 18 months, four up to two years, and one for almost two and a half years.

Two patients are awaiting second stage lobectomy. Both are in good condition.

Forty-one patients have been free from symptoms for periods varying from 16 to 756 days. Of these, 19 have been followed-up for less than three months and 17 have been followed-up for six months or more.

Five patients (one colored woman with nodular goiter, two colored women with diffuse goiter, two colored men with diffuse goiter) have presented varying degrees of clinical hypothyroidism, in one instance with myxedema. Manifestations in all instances, including one patient in whom complete thyroidectomy was done, have been readily controlled with thyroid extract.

Two patients (one colored female with diffuse goiter, one white female with nodular goiter) have presented symptoms suggestive of parathyroid tetany. Both have responded satisfactorily to treatment with calcium, parathormone and vitamins.

Three patients are still toxic. The first is a 44 year old woman with toxic diffuse goiter, followed-up for 160 days after lobectomy; the second stage of operation was refused. Her present basal metabolic rate reading is plus 43. She received thiouracil for 222 days before operation and had an apparent medical cure. The second patient is a 47 year old colored male with diffuse toxic disease complicated by a cardiac factor, who has been followed for 675 days after stage thyroidectomy. When he was last seen his basal metabolic rate reading was plus 46 and he was clinically toxic.

He received thiouracil for 60 days and developed agranulocytosis and leukopenia in the course of treatment. The third patient is a 24 year old white female with nodular toxic goiter. Her history of toxicity extends over four and a half years. She was submitted to stage thyroidectomy in England, and was also treated by stage surgery in Charity Hospital. She developed agranulocytosis and leukopenia after four days of treatment with thiouracil and was prepared for both stages of surgery with Lugol's solution. She bled profusely during the first stage but presented no undue vascularity during the second. At this time, 197 days after operation, her basal metabolic rate is plus 29 and she is clinically toxic.

#### COMMENT

In previous studies of thyroid disease<sup>1, 2</sup> from the New Orleans Charity Hospital we have made the point that this particular condition fully bears out the axiom that any disease is most a problem where it is least a problem. Over the twelve and a half year period ending July 1, 1938, only 952 patients with thyroid disease of all types were operated on in this institution, of whom 50 died; during the same period 53 patients died without surgery. Four hundred twenty of the 952 patients had toxic disease, of whom 38 died after operation. Toxic disease was the cause of 49 of the 53 non-surgical deaths. The most disconcerting aspect of these statistics was that non-surgical deaths in toxic subjects greatly exceeded surgical deaths during the last five years of the analysis. The excess of non-surgical over surgical deaths in the last three and a half years at Charity Hospital is similarly disconcerting.

In former studies, which were chiefly concerned with cases treated at the old hospital, attention was called to the difficulties of preparing toxic thyroid patients for surgery in completely unpropitious and actually antagonistic surroundings, and indeed of treating them at all under the circumstances which prevailed. Overcrowded, noisy wards, often with two patients to a bed, made isolation impossible and increased the patient's emotional instability.

By adequate criteria, even the best prepared patients were poorly prepared and their risk was increased, it was emphasized, by the fact that surgeons, their assistants, anesthetists and nurses all had very little experience with the disease because of the small number of cases which occur in this non-endemic community.

Although conditions are naturally much better in the new and modern Charity Hospital, they are still not ideal for the treatment of toxic thyroid patients. Isolation and bed rest are still impossible of complete attainment. It is perhaps a compromise with reality, but it is nonetheless a real improvement that with thiouracil this strict regimen is no longer carried out. The patient is permitted to be ambulatory, to associate with other patients, and to have as many visitors as the hospital rules permit. The shortening of hospital stay days achieved in private patients treated by thiouracil is not as apparent in Charity Hospital, where, for obvious reasons, out-of-town patients and frequently city patients as well must be prepared for operation in the hospital. The reduction of nursing care, however, is a distinct advantage in this period of extreme personnel shortages.

The number of patients who had reactions from thiouracil in this series, 14 of 58, is somewhat higher than in some reported series, though the numbers are too small to be of statistical value. Fowler and Cole,<sup>5</sup> in an analysis of 1,543 reported cases, found the incidence of reactions to be 13.8 per cent. Their occurrence, as well as the impossibility of preventing them, is granted by all observers to be the greatest disadvantage of thiouracil therapy. They can readily be picked up, however, if observation is adequate, and treatment with penicillin, though the rationale is not entirely clear, seems to have eliminated their chief risk.

Moore<sup>6</sup> suggested that the most dangerous period, from the standpoint of possible reactions, is between the fourth and eighth weeks of therapy. Four of the 14 patients who developed reactions in this series developed them during this time, but two pa-

tients manifested them after four days of treatment and one after five days, while at the other extreme two patients developed them on the eighty-ninth and ninety-first days respectively. The point made by several observers is well taken, that the risk of agranulocytosis is so great that thiouracil should be discontinued several days before operation, lest this serious complication occur without detection in the post-operative period. This precaution was not observed in a number of cases in this series and it is fortunate that no harm resulted from the omission.

The question arises as to whether the 22 lobectomies performed in 13 of the patients in this small series were really necessary. According to Bartels and Bell,<sup>7</sup> at the Lohrey Clinic, where the average of stage operations has been 16 a year, lobectomy was not employed at all in the last year of the period covered by their analysis of 400 thiouracil-treated surgical cases. It may have been that the lobectomies performed at Charity Hospital represented unnecessary caution. On the other hand, the single patient who died was not submitted to stage surgery. Furthermore, three of the five postoperative crises, one of which was very severe, occurred in patients submitted to lobectomy; all three patients survived, but the thought naturally suggests itself that the outcome might have been less happy had more extensive surgery been done. The speculation is not the less significant because one of the three patients was frankly not well prepared and in another case preparation could have been better.

Generally speaking, this series bears out the experiences of most surgeons that thiouracil is a useful agent in the preparation of toxic thyroid patients for operation. We consider it striking, as has already been intimated, that the case fatality rate in males, particularly negro males, which has been prohibitively high in previous studies, is zero in this series, in spite of the extreme toxicity which these patients presented. That the drug was necessary in every instance in which it was used is very doubtful. That it was not used rationally in



every case is evident; some interns and residents merely translated the old habit of administering Lugol's solution to a toxic thyroid patient as soon as he came on the ward to this new agent. Toxic reactions occurred, which were potentially serious, but because they were being looked for, they did not progress to serious stages. The gravest criticism of thiouracil at Charity Hospital, and one which needs no comment, is the fact that, in addition to the patient who died after operation, six patients who were or had been treated with it died under treatment, one on the operating table during induction of anesthesia, the others without surgery. It is only fair to add that this is perhaps not so much a criticism of the agent as of the method by which it was used. Certainly these deaths bear out again the un wisdom and actual folly of submitting to operation patients with rising or stationary basal metabolic rates, regardless of what improvement they may show in other directions.

#### SUMMARY AND CONCLUSIONS

An analysis of 58 cases of toxic thyroid disease treated with thiouracil in preparation for operation at the New Orleans Charity Hospital over the past three years indicates that this drug is a useful adjuvant to the armamentarium in this disease.

The majority of the patients in the series received the drug as a specific part of their preparation for operation. Several cases are included, however, in which it was begun with the idea that operation would not be necessary, a belief that proved fallacious because remission of toxicity was only temporary.

Toxic reactions occurred in 14 of the 58 patients but were not serious because they were promptly detected.

Lobectomies may have been performed in an unnecessary number of cases, but for several reasons the caution which dictated them does not seem unwise.

It is regarded as of particular significance that there were no deaths among the 12 males in this series, although previous studies of toxic thyroid disease from the New Orleans Charity Hospital have shown

a high case fatality rate in males, particularly negro males. It is suggested, however, that the non-surgical fatalities, in several of which thiouracil had been used, must be taken into consideration in estimating the worth of this drug in the treatment of toxic thyroid disease.

Much in this analysis supports the warning of Fowler and Cole<sup>5</sup> that the lessons which have been learned about surgery for toxic thyroid disease in the last three or four decades should not be lightly forgotten in the enthusiasm for a new and still not fully tested agent.

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#### ROENTGENOLOGIC ASPECT OF PNEUMONIAS\*

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and

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Not many years ago, in certain sections of this country, it was customary to give patients with fever 10 grains of quinine every four hours for two or three days, without any laboratory blood examination. This was considered a therapeutic test for malaria. If the fever persisted in spite of this therapy, the conclusion was that the pa-

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tient did not have malaria, but what caused the fever often remained a mystery. Today, it would seem that very much the same procedure in suspected cases of pneumonia is being employed by some physicians. They administer chemical and antibiotic therapy as a diagnostic measure upon the slightest suspicion of pneumonia. If there is no improvement in the condition, pneumonia is ruled out. In many instances, this is an erroneous interpretation. While it may be true that a certain response may be obtained in some bacterial forms of pneumonia, it does not eliminate other types of pneumonia. We wonder whether any one is justified in pursuing such a practice, particularly if a roentgen-ray examination of the chest is available. However, it may be that in certain unavoidable circumstances such a practice has been followed by necessity and not by preference.

The purpose of this discussion is to call attention to many conditions of the lungs which produce a pneumonitis with physical findings and clinical signs which may, at times, be confused with lobar or bronchopneumonia, and which may or may not respond to chemical and antibiotic therapy. Then, too, in some of these conditions physical examination may give but little, if any, early evidence of their presence. The roentgen ray, however, often clearly demonstrates the pathologic process; in some instances, such as bacterial lobar pneumonia, as early as from 18 to 24 hours after its inception, and hours before any diagnostic physical signs are obtainable. In atypical pneumonias, the lesion is usually demonstrated by the roentgen ray within 40 hours after the onset of the disease. It, therefore, becomes possible to detect roentgenographically an early pneumonic process, and also to observe its progress by frequent roentgen-ray studies.

When using the term "pneumonia" in this discussion, it is understood to apply not alone to the two common types of pneumonia, namely, bronchopneumonia and lobar pneumonia, but also to other conditions of the lungs which produce pneumonitis and are visualized roentgenographically as

patchy, lobular or lobar consolidation. Some of these so-called pneumonias are uncommon, while others are of common occurrence. Some are caused by a virus or fungi, etc., however, all of them present interesting medical problems which may confront us at any time.

The conditions which produce pneumonitis with patchy, lobular, or lobar consolidation may be acute or chronic in character and may be due to different causes. In some instances, the clinical findings and physical signs may simulate certain bacterial pneumonias. They are enumerated according to their etiologic factor:

#### *Virus*

1. Primary atypical pneumonia
2. Influenza (epidemic)

#### *Rickettsia*

1. "Q" fever
2. Psittacosis

#### *Bacteria*

1. Lobar pneumonia
2. Bronchopneumonia
3. Tuberculous pneumonia
4. Friedländer's bacillus pneumonia
5. Chronic interstitial pneumonia
6. Streptococcic pneumonia
7. Tularemia
8. Bubonic plague pneumonia
9. Glanders pneumonia

#### *Fungi*

1. Actinomycosis
2. Blastomycosis
3. Aspergillosis
4. Moniliasis
5. Histoplasmosis
6. Torulosis
7. Coccidiomycosis

#### *Protozoan Parasite*

1. Toxoplasmosis

#### *Chemical*

1. Lipoid pneumonia
2. Irritating gas

#### *Circulatory Disturbances*

1. Rheumatoid pneumonia
2. Hypostatic pneumonia

#### *Foreign Bodies*

1. Silicosis
2. Bagassosis



*Allergy (?)*

## 1. Löffler's syndrome

Pneumonia is an inflammation of the lungs and varies roentgenographically according to the kind of lung tissue affected. In this regard, two general types of pneumonia are observed with the roentgen ray, the alveolar and the interstitial. The alveolar pneumonias give a much more dense roentgen shadow than the interstitial form. This results from the air sacs becoming filled with an accumulation of inflammatory exudate, fibrin, fluid and blood, replacing their air content, without collapse of the air sacs, producing an area of consolidation. Since the air sacs now contain substances which absorb roentgen rays in greater quantity than the previously contained air, the resulting roentgen shadow is very dense, and a condition exists which also accounts for the fact that this area becomes dull to percussion, accompanied with altered breath sounds. Then, too, in alveolar pneumonia the bronchi and peribronchial tissues are but slightly affected, which is in marked contrast with the interstitial type of pneumonia. Bacterial lobar pneumonia is a representative type of alveolar pneumonia.

In the interstitial type of pneumonia, the bronchial wall and peribronchial tissues are mainly involved with an inflammatory process, and, in contrast to the alveolar type, relatively little exudate is present in the air sacs. This occasions the patch-like, lobular shadows on the roentgenogram. Then, too, in the interstitial type of pneumonia almost invariably there is some involvement of the regional lymphatic system as evidenced roentgenologically. Bronchopneumonia and some atypical forms of pneumonia may serve as representative types of interstitial pneumonia.

Certain important information may be obtained from the roentgen ray in the study of all forms of pneumonias. For example:

1. To determine whether a suspected lesion is in the parenchyma of the lung, which information is important for an early diagnosis of pneumonia. It is to be recalled that bacterial lobar pneumonia may be diag-

nosed within a very short time after the onset of symptoms, while in other types of pneumonia roentgen evidence of the disease appears less rapidly. On the whole, it may be said that in the earlier stages of pneumonia, the roentgen ray is more diagnostic than physical signs.

2. The roentgen ray is of great help in differentiating certain conditions which, at times, may be confused clinically with pneumonia.

3. To localize and visualize the distribution of a pneumonic process.

4. To determine whether the lesions show roentgen evidence of progression or regression.

5. The roentgen ray is of value in studying the process of resolution, and in determining whether there remain residual processes such as unresolved pneumonia, pleural changes and abscess formation.

6. Whether the pneumonic process is complicated with abscess formation, atelectasis and pleurisy with effusion.

7. Pneumonic processes situated behind the heart, or below the dome of the diaphragm usually give but slight physical signs. The roentgen ray may be most useful in locating such lesions.

It is to be appreciated that there are but few, if any, characteristic physical signs which will give a definite diagnosis of the different types of pneumonia. The laboratory and roentgenographic findings are the most conclusive evidence of the diagnosis. However, it is to be stated that while the roentgen-ray findings are not always characteristic for each pneumonic process, yet in many instances a correct inference as to the disease may result from a study of the pathologic process or processes of these various conditions when affecting the lungs. It is to be recalled that these processes are not always alike, nor do they always affect the same lung structures.

It should be appreciated that the diagnosis of pneumonia is not to be made by a single type of examination, such as the roentgen ray, physical signs, blood and

sputum examinations, but by the combination of all known factors.

The roentgenologist serves best as a medical consultant when he is given all the clinical data appertaining to the case. In this manner, the referring physician may receive important diagnostic information concerning his patient, particularly when the roentgenologist has examined a patient suspected of having pneumonia.

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## CONGENITAL HEMOLYTIC JAUNDICE

### A CASE REPORT WITH SPLENECTOMY IN FATHER AND SON

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Congenital hemolytic jaundice is a chronic disease with familial tendency that appears to follow a mendelian pattern. It is a disorder of the red blood cell physiology characterized by chronic anemia, increased fragility of certain of the red cells, jaundice of the acholuric type, urobilinuria, hyperplasia of the erythroid elements in the bone marrow, hereditary trait and splenomegaly. In its cycle there may be acute crises due to extensive destruction of the red blood cells, and in its course, may be complicated most frequently by cholecystitis and cholelithiasis.<sup>1, 7, 13</sup>

Of all the blood dyscrasias associated with splenomegaly, congenital hemolytic jaundice is the most completely identified. It was first recognized by Murchison in 1885 and fully discussed in detail by Hayem in 1898. The familial characteristics of the disease were described by Minkowski and the increased fragility of the red blood cells and the large number of microcytes and reticulocytes were observed by Chauffard. Haden has shown quite conclusively that the increased hemolysis is due to the presence of a large number of spheroidal shaped red cells which are pathognomonic of the disease, and which are more easily hemolyzed than the normal bi-concaved discs. He explains this feature on the basis of lessened ability of the spheroidal cell to stretch more than the normal bi-concaved disc. Krumbhaar has suggested that the disease

be called spherocytic jaundice since the inherent defect is due to a spherocytosis. Until the cause for the presence of the spherocytosis be determined, it is wiser not to confuse the picture by still another name as this disease already has innumerable labels.

A similar condition which has been described as an acquired type, is now believed to be the congenital form but which has been dormant and has been activated by superimposed diseases. Upon investigation, other members in the family group have been found to have the disease.

The splenomegaly which is constantly present is not a primary factor and is considered due entirely to the increased function of destroying the incapacitated cells and removing the debris from the circulation. Theoretically it would appear that splenectomy would permit a longer life to the spherocytes, permitting the bone marrow to resume a more normal function. However, it has not been demonstrated that the spleen is the cause for the increased hemolysis. It is more likely that the increase in hemolysis is an *in vivo* duplication of an *in vitro* experiment, namely that the variations in the ingestion of water and salt may play a determining role. These splenectomized patients continue to show periodic jaundice and variations in the red blood cell counts. These recurrences are postulated as being due to accessory splenic tissue or to the assumption by the hemolymph nodes of the phagocytic function of the spleen.<sup>9</sup>

Under certain circumstances, the demand for more red blood cells is so great that the function of the bone marrow to keep up becomes disrupted and immature red blood cells and white blood cells appear in the circulation. During these episodes, the patient appears in crisis with severe anemia, fever, abdominal pain and accentuation of the jaundice. No cause for the onset of these crises has been found. It is difficult to explain these crises on the basis of a congenital disturbance in the red blood cell formation. There are numerous reports of several members of a family, suffering from this disease, who have had crises,



within a very short period of one another. This would suggest an extrinsic factor as the initiating cause of the acute hemolysis. The predominating features are the great increase in circulating spherocytes, increased blood destruction and jaundice that resemble the toxic reactions of chemical or immunologic substances, previously introduced.<sup>2, 4, 5</sup>

The symptoms and physical findings are to a large measure dependent upon the severity and chronicity of the disease. In the quiescent form, there may be no symptoms other than the anemia or mild icterus, and upon examination splenomegaly, increased fragility and spherocytosis are found. No two patients may have the same group symptoms. The jaundice is not very deep. The icteric index is seldom more than 40. The urine is deeply colored but the color is due to urobilin and not bilirubin. In congenital hemolytic jaundice the stools are normal in color which distinguishes it from obstructive jaundice.

Acute exacerbations of the disease are described as crises. Lippman states that crises are not frequently reported in children and are usually overlooked. Mandelbaum reports an initial hemolytic crisis in a man aged 75 with all the diagnostic signs in whom a splenectomy was performed followed by recovery. The onset may be rapid with weakness, pain in the upper abdomen, fever from 100 to 104°, nausea and vomiting. The weakness may increase to prostration and coma. The jaundice deepens and upon examination the red cell count is found to be as low as one million. The smear is found to contain immature red and white cells. The resistance of the red cells to hypotonic saline is reduced. The tenderness is due to a congestion of the spleen. Patients in crises must be given repeated transfusions besides general therapeutic measures so that splenectomy may be performed and when the anemia cannot be satisfactorily handled, emergency splenectomy has been resorted to with recovery.<sup>1, 3, 6, 8</sup>

Cholecystitis and cholelithiasis are frequent findings in long standing cases of hemolytic jaundice. Ashby reports finding

two gall stones in a child age 14 months upon whom he performed a splenectomy. In this case the gallbladder was not removed but the child's mother had had a splenectomy and cholecystectomy for gall stones. Sharpe states that gall stones occur as a complicating factor in 63 per cent of cases and the calculi are the pigmented type. It is generally believed the increased incidence of gallbladder calculi is due to the increased hemolysis. In the normal blood, hemolysis usually begins in salt solution of 0.44 per cent and is complete at 0.36 per cent. In chronic cases, the hemolysis may begin at 0.6 or 0.7 per cent and may even be complete at 0.7 per cent. The increase in the amount of free hemoglobin passing through the liver results in an increased output of pigment which becomes deposited in the gallbladder.<sup>6, 10, 11, 12, 14</sup>

Another occasional observation seen in chronic hereditary jaundice is a peculiar osseous change noted in thickening of the frontal and occipital bones which Cooper has described. He noted that the bones of the cranium as well as elsewhere showed a dense cortex. This thickening, he believes, is due on the one hand to the active hyperplasia of the bone marrow and formation of new bone and on the other to the exhaustion of the overstimulated marrow and replacement of the degenerating cells by fibrous tissue. This deformity of the skull gives to some patients a mongoloid facies as was noted in the boy recorded in this paper. This mongoloid appearance has also been seen in erythroblastic or Mediterranean anemia and in sickle cell anemia and hence is not pathognomonic.<sup>15</sup>

Chronic indurated ulcers of the leg have been described as associated with chronic hemolytic jaundice which were intractable to treatment and only were healed after splenectomy.<sup>16</sup>

It is universally agreed that splenectomy offers the only permanent relief of the symptoms. It should be recommended even in the latent or symptom-free cases because of the potential danger of a superimposed crisis. It is recognized that during an acute crisis, every effort should be made to pre-

pare the patient for operation by means of transfusions and chemotherapy. There have been reports of splenectomy being performed in the acute phase wherein every effort to put the patient in suitable shape were unavailing and splenectomy had to be done with uneventful recovery.

Although it is generally stated that following splenectomy the clinical signs and symptoms do not reappear, this must be doubted because the tendency to increased fragility is still present and the spherocytosis remains. Splenectomy does not change these. Patients continue to show mild degrees of jaundice and fatigue. At times urobilin is found in the urine. Crises may not be as frequent but they do occur and are explained away by declaring that the other lymphoid tissues have taken over the phagocytic activity of the spleen.

#### CASE NO. 1

W. H., a white male aged 25, was first seen on April 10, 1934, with chief complaints of jaundice and weakness.

For the previous four weeks he had been having attacks of precordial pains with palpitation. His legs would become weak and he would break out in cold sweats. The appetite had become poor. The bowels were regular and normal. No blood was seen in the stools. His weight has been constant. For a long time he has noted that he was jaundiced and this jaundice, which was not very intense, would vary from time to time. He never noted any blood in the urine, although the urine has been very yellow at times. He sleeps poorly.

The past history revealed he had been having these weak spells with jaundice since the age of 13, and he was also subject to tonsillitis.

He is married; wife living and well; one child living and well. One premature child who died with jaundice. See chart of family history.

Physical examination reveals a thin, slightly icteric white male who appears definitely sick. The sclerae are yellow but not deeply so. The head, ears, nose are negative. The mouth shows recent wounds from dental extractions. There are several teeth left and these are very badly decayed. The gums are swollen and markedly pyorrheic. The skin is pale lemon yellow color. Temperature 99.6, pulse 96, respirations 20. The heart is normal in size and no murmurs are detectable. The lungs are negative throughout. The skin of the abdomen reveals a costal varicosity of the spider burst type. The spleen is enlarged. It extends upwards to the eighth rib in the midaxillary line and anteriorly to the left mammary line and downward to the crest of the ilium. The edge is round

and the notch is palpable. It is freely movable. The liver edge could not be felt. No other masses are palpable. The lymph nodes are not enlarged.

Laboratory reports: Urine—yellow, clear, acid, sp. gr. 1.025, no albumin or sugar present. Urobilin 3 plus. Microscopic—few hyalin casts. Blood—hemoglobin 70 per cent; red blood cells 3,216,000, white blood cells 10,000. Schilling index—B-O, E-O, M-1, J-2, St-4, S-58, L-35, M-O. Smear—many micro and macrocytes with polychromatia. Stools—soft greenish brown. No ova or parasites. Kahn—negative. Clotting time—three minutes. Icteric index 15.0. Sedimentation rate—3 in 60 minutes. Fragility test—complete hemolysis at 0.44 per cent NaCl.

A diagnosis of congenital familial jaundice was made and splenectomy advised but was refused for two years. During this period the patient was under constant attention. Numerous blood studies were carried out comparing the icteric index with the red blood cell count and the fragility tests in order to determine what would cause these crises. The only conclusion that appeared to explain this phenomenon was that the intake of large volumes of liquid seemed to increase the frequency of the attacks of feeling badly. As a result the patient was placed on a liquid restricting diet.

In December 1936 he went to the Mayo Clinic where he was examined and the diagnosis confirmed and splenectomy advised. The laboratory findings were essentially the same as those reported above.

Upon his return, operation was performed under ether and ethylene. Through a left rectus incision the spleen was easily mobilized and a mass ligature placed about the pedicle and the spleen removed. No difficulty was encountered. The spleen weighed four and a half pounds. Postoperative convalescence was uneventful and he was discharged in one week.

A section of the spleen was sent to Dr. Broders who returned the following report: Chronic splenitis with fairly marked increase in fibrous connective tissue, thickened capsule, marked decrease in number of Malpighian bodies with thickening and hyalinization of the vessels of those that remain. The picture was not that which we see most frequently with hemolytic jaundice. There was evidently more connective tissue present and a thickened capsule together with more destruction of Malpighian bodies than we usually see.

Since the operation he has continued to show varying degrees of icterus. The icteric index of the serum is still higher than normal and varies in amount from time to time. X-rays of the gall-bladder on several occasions demonstrated no pathology.

#### CASE NO. 2

M. L. H., a white male aged 8, the son of Case 1, also had jaundice. The child was first seen at seven months of age, because of fever. At this



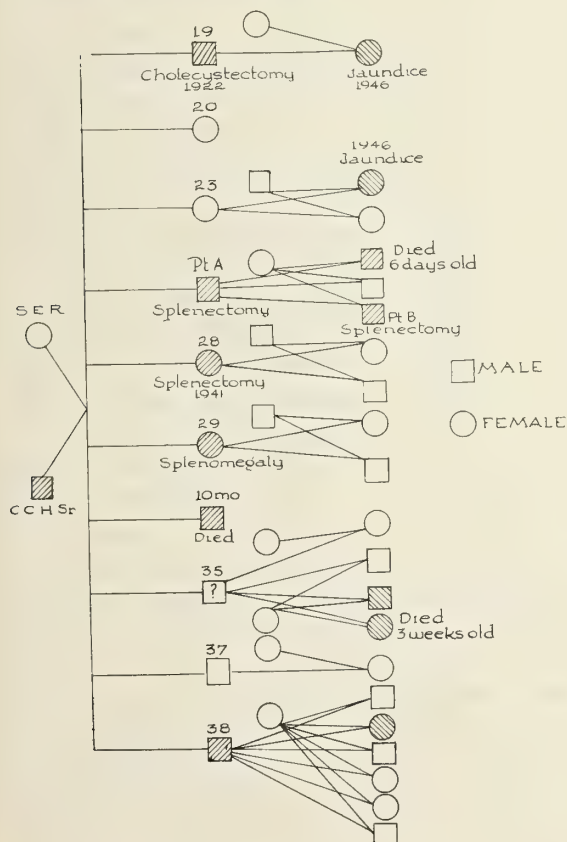
time it was noted that the child was almost milk white in color with a tinge of yellow. He was not in pain. The abdomen was distended and the superficial vessels were prominent. The spleen was enlarged and extended three finger breadths below the costal margin on the left. The liver was not palpable. There was no lymphatic enlargement. The facies was suggestive of a Mongolian type.

He was not seen again until four years later. At this time the spleen was found to be considerably larger. He was more definitely icteric. The urine did not contain any urobilin. At this time the hemoglobin was 60 per cent, red blood cells 3,700,000, white blood cells 10,400. Schilling index—B-2, E-4, M-5, J-1, St-0, S-16, L-72, M-O. On the smear the cells showed an aniso-poikilocytosis, achromia and several nucleated red blood cells. Fragility tests presented complete hemolysis at 0.44 per cent NaCl.

Again he was lost sight of for four years when he was again seen because of temperature 105°. He was pale and slightly icteric. The spleen had grown considerably larger. There had been attacks of pain in the abdomen with cramps. The stools were normal in color. The appetite had remained good. His weight was 59½ pounds.

The past history revealed he had had frequent attacks of abdominal pains with fever.

Family history—See chart.



Physical examination showed the skin to be pale and icteric. The mucous membranes of the mouth and conjunctivae had a watery appearance. The tonsils were large. No lymphatic enlargement of the neck, axillae or groin was present. The spleen was palpable to the umbilicus. The edge was rounded. The liver edge could not be felt. There was a soft mitral systolic and diastolic murmur present in the left second interspace which was considered to be hemic.

A diagnosis of congenital familial jaundice was made and as his condition was becoming progressively worse, the parents consented to operation. He was accordingly prepared for splenectomy.

Red blood cells 2,866,000 with marked microcytosis, white blood cells 7,900 P-52, L-42, M-6, hemoglobin 30.5 per cent or 5 grams. Fragility began at 0.44 per cent and was complete at 0.38 per cent NaCl.

He received 500 c.c. of whole blood every three days until his hematology was within normal limits and a splenectomy was performed on September 5, 1944. The spleen was easily mobilized through a left upper rectus incision. The pedicle was freed and a ligature placed around it. A transfixion suture was likewise placed and the spleen removed. The wound healed per primam and his convalescence was uncomplicated. He was discharged from the hospital on the eighth day.

Since his operation, he has remained free from the former bouts of high fever but he still shows a tendency towards icterus at times. The facies no longer appears mongoloid. Whether this change has been due to growth or to the operation is hard to tell.

Pathologic report of Dr. J. M. Miles: The specimen is that of a spleen which measures 18 cm. long, 9 cm. wide, and 4 cm. thick. The cut surface is smooth and of a deep red color resembling that of raw liver. No pulp could be scraped from the cut surface. The microscopic section shows the spleen to be engorged with red blood cells causing the lymph follicles to appear small and decreased in number. The gross and microscopic appearance is that of the spleen of hemolytic jaundice.

#### SUMMARY

1. A report of the results of splenectomy in the treatment of congenital familial jaundice occurring in father and son, with a record of its appearance in three generations, is recorded.

2. A review of the pertinent features in the clinical, pathologic and surgical treatment of the disease is presented.

3. The course of the disease, while considerably improved by splenectomy, is not terminated thereby, but recurs in a milder

form intermittently, depending upon the water and salt intake.

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## SADDLE BLOCK ANESTHESIA IN OBSTETRICS\*

### A PRELIMINARY SURVEY OF 50 CONSECUTIVE CASES\*\*

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AND  
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NEW ORLEANS

The term "saddle block" is employed to designate a low spinal anesthetic, with the effects confined chiefly to the perineal region. It has been used for several years in proctology and in cystoscopy. Adriani suggested its use in obstetrics in New Orleans and has published several valuable contributions based on his experience.

We have resorted to this method of anal-

\*Read before a meeting of the Orleans Parish Medical Society, April 14, 1947.

\*\*From collected cases of Dr. E. L. King, Dr. John S. Herring and Dr. Isadore Dyer.

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gesia with increasing frequency in the past two years, and in this preliminary report we wish to present our experiences in one hospital during the past six months. We feel that an analysis of consecutive cases in one institution with uniformity of nursing care, gives a better opportunity in evaluating the results. In this period of time, we delivered 98 patients vaginally in this hospital; in 50, saddle block was used, and in 48 it was not employed.

The technic advocated by Adriani has been modified in this series and the following method was used:

#### Necessary drugs:

- 1 ampoule 3 c.c. 10 per cent glucose.
- 1 ampoule 2 c.c. containing 10 mg. Nupercaine (1/200)
- 1 ampoule adrenalin (optional)
- 1 ampoule 1 c.c. 5 per cent ephedrine with 1 per cent procaine.
1. Wash 5 c.c. syringe with 1 c.c. 10 per cent glucose and repeat, using another 1 c.c. (this leaves 1 c.c.).
2. Wash same syringe with 1 c.c. Nupercaine.
3. Now mix remaining 1 c.c. 10 per cent glucose with 1 c.c. Nupercaine (5 mg.) and 1/2 c.c. adrenalin (this is used for spinal injection).
4. With ephedrine—procaine solution, infiltrate skin of back and make a lumbar puncture with the patient sitting up. Use either L 3 or L 4.
5. Insert spinal needle, and when in canal, inject solution (3) mixed above, just after patient has completed a contraction. Inject at a rate of 1 c.c. per second.
6. Keep patient sitting up for 90 seconds then lie flat, with head elevated on pillows.

Analgesia is established within three to five minutes, and is manifested chiefly by a complete abolition of the pain of uterine contractions. If properly given, the anesthesia extends to, or slightly below the level of the umbilicus, associated with partial or complete loss of motor function of the lower extremities. Most patients, however, can move the toes and flex the knees. The ef-



fects persist from two to four hours, frequently longer, so that the majority do not require additional gas anesthesia for delivery. At times there is a temporary lessening of the force and frequency of the uterine contractions, but this effect soon wears off, unless the "block" is administered too early in labor. There is a tendency for the presenting part to recede somewhat in the birth canal. Voluntary urination is inhibited, necessitating careful vigilance of bladder retentions and catheterization during labor. Due to the relief of pain, the patient is not aware of the uterine contractions, which are soon back to normal and hence does not use her abdominal muscles as aids to delivery, unless coached by the physician or by a nurse. There is relaxation of the structures of the pelvic floor and vagina, (and to some extent the cervix is involved), and this relaxation, together with the diminished voluntary expulsive force, tends to retard moulding of the head and anterior rotation of posterior occipital positions. This retardation is in direct ratio to the degree of cephalo-pelvic disproportion, which is also the case to a less degree when saddle block is not used. Due to the "fortification" of the anesthetic mixture with adrenalin and the administration of ephedrine in the skin wheal, little or no fall in blood pressure is noted. Should this develop, it is early and transient: 10 to 15 per cent of the patients develop nausea and vomiting within the first hour; the mechanism of this is not well understood.

The analgesia should be administered when labor is well established, with satisfactory contractions occurring two to four minutes apart; the cervix should be at least 75 per cent effaced, and 6 to 8 cm. dilated in a primigravida and 4 to 5 cm. dilated in a multigravida. The presenting part should be at the level of (or below) the ischial spines, and definite progress should have been observed during the hour before administration. If necessary, preliminary drug analgesia is administered until the proper stage is reached.

The 50 patients forming the basis of this report comprise 36 primigravida and 14

multigravida. In 14, there was noted cephalo-pelvic disproportion of 100 c.c. or more at the mid-plane. All babies presented by the vertex; in 20 the occiput was anterior when the block was administered, in 23 it was posterior, and in seven the sagittal suture was lying transversely. At delivery there were 28 anterior positions, seven transverse, and 15 persistent posterior positions. These later were rotated by forceps. Forty-nine of the 50 cases delivered by forceps, of which 37 were low and 12 were midforceps; four done because of fetal distress, four because of deep transverse arrest, four because of persistent occipito-posterior positions. There was no fetal or maternal mortality. There were three cases (6 per cent) of postpartal complications, namely, one case each of mastitis, pulmonary atelectasis and retained secundies. None of these could be attributed to the saddle block. There was no postpartal hemorrhage. The analgesia was satisfactory in every patient. The duration averaged three and a half hours. In three patients the block was administered too early, due to error in estimating cervical dilatation; their labors stopped for several hours. In one of these patients the block was later repeated with satisfactory results. In seven patients, labor lasted four or more hours after the block was administered; 40 were delivered in less than four hours. Approximately 30 per cent required a light gas anesthesia at time of delivery, but retained enough analgesia for perineal repair without gas.

Forty-five babies cried immediately at birth. Five required resuscitation, but none was deeply asphyxiated. In one instance, fetal distress was present prior to delivery, the cord was found to be twice around the neck and rather tightly drawn. We believe that the asphyxia in the other four babies was due to the administration of analgesic drugs prior to the saddle block, plus the use of gas anesthesia at the time of delivery.

Postpartally, we find that 15 patients required catheterization once at the end of

eight hours. Two of these were also catheterized again at the end of the second eight hours. Two other women had persistent urinary retention, and were treated by the use of indwelling catheters; one for 24 hours, one for three days. There was no incidence of cystitis. We have learned that it is very important that the bladder be completely emptied by voiding not later than eight hours after delivery. It is essential that the nursing staff be instructed as to the importance of this detail, otherwise overdistension of the bladder with subsequent bladder atony and retention is almost inevitable.

#### POINTS TO BE STRESSED

1. Saddle block anesthesia is to be used only in a hospital and should be given by a trained anesthetist. It is applicable to about 50 per cent of patients.
2. Many primipara will go entirely through the first stage of labor without need of analgesia; many multipara have such rapid labors that this anesthesia cannot be used. It definitely should not be used too early in labor.
3. Labor must be well established, there must be cervical effacement and dilatation or cessation of labor will result.
4. It should not be regarded as an analgesia for the early part of the first stage of labor. Definite retardation of moulding of the fetal head, rotation of posterior positions and descent, in patients with moderate to marked cephalo-pelvic disproportions can be expected when the block is used.
5. It is important to keep the bladder emptied during labor, and watched for the first eight hours after delivery.
6. Saddle block anesthesia is better than heavy sedation, and gas anesthesia for delivery, as far as the baby is concerned.
6. Although there is a tendency for spontaneous rotation to be retarded, relaxation of the soft parts facilitates forceps procedures.
7. If saddle block anesthesia is contemplated, it is essential that the obstetrician be sufficiently trained to evaluate the progress, and changes during labor, have sufficient knowledge of cephalo-pelvic rela-

tionship and be prepared in any event to conduct a skillful forceps delivery.

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### THE HUTCHINSON MEMORIAL CANCER DETECTION CLINIC

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Although cancer has been recognized as a disease for many centuries, it was not until 1802 that the first cancer society was established. A group of English physicians made an attempt to understand more of this disease by circulating a questionnaire to the profession in the hope that important observations would aid in solving the cancer problem. Unfortunately nothing seems to have been accomplished.<sup>1</sup> In Koenigsberg, East Prussia, a physician by the name of Georg Winter established an educational campaign in the 1890's to acquaint women with the early symptoms of cancer of the uterus and to advise them to seek medical care when these symptoms appeared.<sup>2</sup> A similar program was initiated in this country in 1914 when the American Society for the Control of Cancer was founded. From the beginning this group has publicized the signs and symptoms of early cancer in an attempt to arouse the public awareness of this disease. It is because of programs such as this that cancer is no longer considered to be a shameful disease, but one that may be discussed freely with the physician and others. The trend of the educational effort now is away from teaching the symptoms of early lesions to that of advising periodic health examinations, for it is well known that when patients notice symptoms the disease already may be advanced too far to hope for successful cure.

In an attempt to discover early lesions, Dr. Elise L'Esperance, of the New York Infirmary for Women and Children, established in 1937 the first clinic designed to perform periodic complete health examinations on women who had no symptoms of cancer. The first series reported by that clinic<sup>3</sup> showed the incidence of malignan-

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cies to be 7.6 per cent of 1800 women examined. Most of the tumors were early and, therefore, offered a good prognosis with proper treatment. In 1938 a clinic was founded by Dr. Catharine Macfarlane and others at the Woman's Medical College of Pennsylvania to determine the value of periodic pelvic examinations in the discovery of early lesions of the female genital tract. The intention was to find presumptive, not definitive, evidence of cancer.<sup>4</sup> Because of the excellent results of these clinics, others of similar pattern have been organized throughout this country.

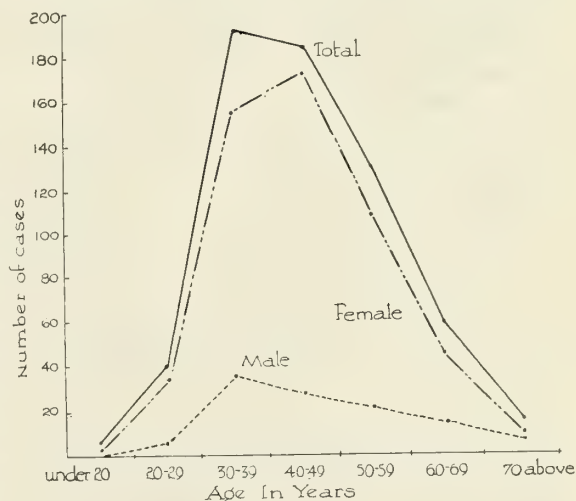
On March 1, 1946, a cancer detection clinic was opened at the Hutchinson Memorial Clinic of the Tulane University School of Medicine, under the auspices of the Orleans Parish Medical Society and the American Cancer Society. This clinic has recently completed one year of operation and it is believed that the findings are of interest and may stimulate other groups to establish similar clinics.

The clinic staff consists of three internists, two gynecologists, one surgeon, one or two nurses, a secretary-receptionist, and a laboratory technician. Because the facilities of the Hutchinson Clinic are available, it is unnecessary to provide separate apparatus for x-ray, proctoscopic, or other more detailed examinations. The clinic operation is governed by standards established by the American Cancer Society, so that biopsies or therapeutic measures are not performed in the clinic, but by the physician of the patient's choice. No selection has been made as to sex, color, or age, but an attempt has been made to exclude any one who is under treatment for cancer or who has definite symptoms of this disease. It is intended that repeat examinations will be accomplished at intervals of approximately six months. If the patient feels that he is able to pay, a contribution of five dollars is made, which amounts to approximately one-fifth of the total cost of the examination. The deficit is financed by funds from the American Cancer Society.

The clinic is open for two hours twice weekly and nine patients are seen each day.

This means that the internist can average forty minutes with each patient. The gynecologist has found it necessary to spend at least twenty minutes on each examination. This includes a gynecologic and obstetric history, bimanual pelvic, colposcopic, and rectovaginal examinations and the taking of vaginal and cervical smears to be stained by the Papanicolaou method. The surgeon is the last to see each patient and, in addition to examining the breasts, may do any other procedures requested by the internist. In some instances it is necessary to spend more time if the history or physical findings suggest that a malignancy is present.

During the first year 636 patients were seen for the first time. Of these, 597 were white, 39 colored, 527 female, and 109 male. It is interesting to note that there were more patients in the fourth decade than in the fifth decade (fig. 1). This would



seem to indicate that the public has become aware that cancer is not necessarily a disease of later life.

Of this group there were 77 patients with 98 lesions considered to be probable cancer, possible cancer, or precancerous, according to the impression of the examiner. These are tabulated by region involved (table 1). In addition, there were 23 women who had vaginal or cervical secretions which were positive for cells suggestive of malignancy when stained by the Papanicolaou method. Nine of these patients had other lesions and

TABLE 1

Lesion	Cancer		Precancerous	Total
	Probable	Possible		
Skin and appendages.....				20
Basal cell carcinoma.....	3	1		
Squamous cell carcinoma.....	1			
Leukoplakia of lip.....			2	
Intraductal papilloma of breast.....			2	
Carcinoma of breast.....	3	8		
Respiratory system.....				3
Bronchogenic carcinoma.....	1			
Laryngeal carcinoma.....		2		
Hemic and lymphatic systems.....				4
Hodgkin's disease.....		1		
Parotid carcinoma.....		1		
Leukemia.....		2		
Digestive system.....				6
Carcinoma of stomach.....		1		
Rectal polyp.....			3	
Abdominal mass.....		2		
Endocrine system.....				5
Thyroid carcinoma.....	2	3		
Genitourinary system.....				60
Vestibular leukoplakia.....			9	
Carcinoma of vulva.....		2		
Carcinoma of clitoris.....		1		
Cervical polyp.....			1	
Cervical leukoplakia.....			18	
Cervix, suspicious lesion.....		6		
Cervical carcinoma.....	4	14		
Ovarian tumor.....		3		
Carcinoma of uterine fundus.....		1		
Carcinoma of testis.....		1		
Total.....	14	49	35	98

are included in the group of 77. The other 14 patients showed no clinical evidence of cancer.

Twenty-eight patients had more than one lesion which was considered malignant or premalignant (table 2). This adequately

TABLE 2  
MULTIPLE LESIONS

	Number of Patients
Possible and probable .....	2
Possible and premalignant .....	12
Possible and positive Papanicolaou stain.....	2
Probable and premalignant .....	2
Probable and positive Papanicolaou stain.....	4
Premalignant and positive Papanicolaou stain .....	2
More than one possible .....	1
More than one probable .....	0
More than one premalignant .....	3
Total Number of Patients .....	28

demonstrates that it is necessary to perform a complete examination rather than to be satisfied by the discovery of one lesion.

The physician designated by the patient was sent a form on which he was asked to indicate further diagnostic procedures performed by him and his final diagnosis. The response has been very favorable, for 78, or 86 per cent of the follow-up forms have been returned. Ten cases of microscopically proved malignancies have been reported. An additional case was given a final diagnosis of carcinoma of the breast, but was considered inoperable by the physician. This total of 11 malignancies is an incidence of 1.73 per cent in all patients examined. Ten of these patients came from the group which had lesions considered as probable cancer.



TABLE 3  
MALIGNANCIES

Color	Sex	Age	Clinical Diagnosis	Comment	Pathologic Diagnosis
W	F	72	Suspicious lesion of nose, and positive Papanicolaou	Nasal lesion excised; refused D and C or biopsy of cervix	Basal cell carcinoma of nose
W	M	45	Squamous cell carcinoma of thigh	Excision biopsy	Early epidermoid carcinoma
W	M	58	Bronchogenic carcinoma	Died	Primary bronchogenic carcinoma
C	F	48	Cervical carcinoma and positive Papanicolaou	Biopsy; radium therapy	Squamous cell carcinoma
W	F	65	Carcinoma of breast	"Lesion inoperable"	Carcinoma of breast
W	M	32	Basal cell carcinoma of nose	Excision biopsy	Basal cell carcinoma
W	F	64	Carcinoma of cervix and positive Papanicolaou	Biopsy; radium	Carcinoma of cervix, Stage III
C	F	34	Carcinoma of cervix and positive Papanicolaou	Biopsy; radium	Carcinoma of cervix, Stage II
W	M	58	Basal cell epithelioma of temple	Excision biopsy	Basal cell epithelioma
W	F	67	Carcinoma of breast; leukoplakia of vulva	Radical mastectomy; vulva not biopsied	Scirrhus carcinoma; no lymphadenopathy
W	F	47	Possible carcinoma of the cervix	Biopsy; radium	Squamous carcinoma of cervix, Stage II

The findings in the remaining 67 patients who were followed are of interest. Thirteen went to their physicians, biopsy or a surgical procedure was done, but no evidence of malignancy was found. Eighteen patients did not report, so the diagno-

sis has not been established. Therefore, out of 60 patients who reported to a physician, 36, or 60 per cent, received no further diagnostic procedure and the final diagnosis is unknown. A brief summary of representative cases is given in table 4. In contrast

TABLE 4  
LESIONS INADEQUATELY TREATED

Clinical Diagnosis	Clinical Description	Treatment Refused*	Treatment after Referral
Possible carcinoma of cervix	Cervix hardened and cystic with small granulation at external os		D and C recommended; patient refused
Leukoplakia of vulva; possible carcinoma of vulva and cervix	Rock hard mass in right labium majus underlying an area of leukoplakia. Polypoid lesion of cervix		Patient refused treatment
Probable carcinoma of thyroid	5 x 3 cm. mass with several stony hard areas		Patient refused treatment. Had not the time or money to be treated
Carcinoma of the uterine fundus; nodules in breast	Endocervix widely patent; uterus enlarged; three hard nodules in breast; biopsy indicated		Patient refused treatment
Patients with Positive Papanicolaou**			
Positive Papanicolaou	Cervix appeared normal but bled after passage of sound		No biopsy or D and C
Positive Papanicolaou; endometrial polyps	Endocervix dilated with small cluster of endometrial polyps		No biopsy or D and C; "observation"
Patients Inadequately Treated***			
Possible carcinoma of breast	Hard mass which did not transilluminate and felt partially fixed to surrounding tissue, but not to skin. Excision and frozen section indicated		No biopsy

(Continued on Next Page)

TABLE 4—Continued

Clinical Diagnosis	Treatment Refused*	Treatment after Referral
Possible carcinoma of cervix	Marked laceration; several friable bleeding areas on anterior lip; hospitalization indicated	Patient examined but no biopsy done
Carcinoma of cervix, Stage I; leukoplakia of cervix	Cervix 3 x normal size, cystic and red; contact bleeding	Biopsy suggested but patient did not return
Leukoplakia of vulva	Same, with obliteration of interlabial folds; splitting of fourchette on gentle examination	No biopsy

\*Two similar cases not included in table; \*\*five similar cases not included in table; \*\*\*18 similar cases not included in table.

to this group are the 24 patients who received adequate examination; 11, or 45.8 per cent, had proved cancer.

Had there been no cases of cancer in this series, it is felt the operation of this clinic has been justified for the many non-malignant, but nevertheless serious, conditions which have been discovered. Many of these are amenable to treatment. The more important are listed in table 5.

TABLE 5  
MISCELLANEOUS CONDITIONS

1. Diseases of the body as a whole	
Possible rheumatic fever .....	1
Nutritional deficiency .....	7
Amebiasis .....	1
2. Diseases of the integument and associated tissues	
Sebaceous cyst .....	15
Lipoma .....	14
Papilloma .....	21
Dermatitis venenata .....	5
Cystic breast disease .....	86
3. Diseases of the musculoskeletal system	
Arthritis—all types .....	30
Ganglion .....	2
4. Diseases of the respiratory system	
Bronchitis .....	3
Bronchial asthma .....	2
Tuberculosis—active .....	3
5. Diseases of the cardiovascular system	
Hypertensive cardiovascular disease.....	11
Arteriosclerotic heart disease .....	9
Rheumatic heart disease .....	4
Hypertension, cause undetermined .....	63
Varicosities, leg .....	59
Thrombophlebitis, leg .....	2

6. Diseases of hemic and lymphatic systems	
Anemia (less than 75 per cent hemoglobin) .....	88
Obstructive parotitis .....	1
7. Diseases of the digestive system	
Splenomegaly .....	4
Hepatomegaly .....	34
Gallbladder disease .....	8
Rectal polyp .....	6
Hernia—all types .....	24
Anal fistula .....	5
Hemorrhoids .....	146
Peptic ulcer .....	4
8. Diseases of the urogenital system	
Urethritis, purulent, female .....	1
Pyelonephritis .....	2
Cervical erosion, severe .....	40
Cervical polyp .....	19
Possible endometriosis .....	6
Uterine prolapse .....	33
Leiomyomata of uterus .....	72
Ovarian cyst .....	26
Cystocele .....	188
Rectocele .....	159
Early pregnancy .....	3
9. Diseases of the endocrine system	
Diffuse thyroid hyperplasia .....	9
Possible thyrotoxicosis .....	4
10. Laboratory	
Urine—voided	
Albumin .....	10
Sugar .....	13
Casts .....	13
Red blood cells .....	72
Positive Kahn and/or Wassermann .....	5
Lymphocytosis .....	1

COMMENT

The purpose of the cancer detection clinic is to influence individuals, both medical



and non-medical, to accept periodic health examinations as the best available method for the control of cancer. The response of the public has been excellent and has enabled clinics such as this to demonstrate that the time and effort expended are extremely productive of early lesions of malignant nature. However, such measures are not limited to clinics of this type, but may be employed by the individual practitioner. It is imperative that he be suspicious of apparently benign lesions, for physicians have told patients that such lesions are no cause for alarm and that a re-examination will be done at a later date. During this period of procrastination the lesion may advance so that only palliative rather than curative therapy can be instituted. Episodes such as this are not uncommon, for it has been shown in this series that 60 per cent of all patients with lesions suspected of being cancerous, who have been referred from this clinic to their physicians, have received inadequate treatment or none at all.

## SUMMARY

1. The Hutchinson Memorial Cancer Detection Clinic has recently completed one year of operation.
2. Six hundred and thirty-six well patients were seen for the first time.
3. Ninety-one patients had lesions suspected of being cancer.
4. Thirteen patients had lesions which were suspected of being cancer, but when biopsy or surgical procedures were done they were proved to be benign.
5. Eleven patients had proved carcinoma.
6. Sixty per cent of patients who reported to their physicians with suspicious lesions did not receive the benefit of further diagnostic procedures.
7. Periodic complete examination of all individuals is the only method by which early cancer may now be detected.

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## IMPOTENCE\*

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Although a wealth of literature has accumulated related to the psychologic, psychiatric, psychosomatic, and urologic problems concerning modern warfare, there has been negligible attention paid to the subject of impotence. Impotence, a matter of considerable personal concern to the patient, promises to be of major importance among veterans of World War II if the experiences of the writer are a reasonable indication of the prevalence of this condition.

This report is based upon my military experience with 22 men (16 officers and six enlisted men) who were referred to me because of impotence. The youngest patient was 20 years old; the oldest patient was 33 years old. Without exception, all of these men were in excellent physical condition.

All of the patients presented histories of having been potent prior to going overseas. Three of the patients observed a loss of their potency while they were overseas. Many of these men had ascribed their impotency at that time to the fear of acquiring a venereal disease and had dismissed the matter as being a sound commentary on their personal background and will power. Fourteen of the entire group had been relieved from active duty at some time for operational fatigue but this condition had been transient.

One or more reasons for his impotence were named by each of the patients. These were as follows:

1. Diets deficient in fresh vegetables, fruit, meat, eggs, and milk caused testicular atrophy (10 cases).
2. Inadequate oxygen intake during high

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altitude flying caused the testicles to die (six cases).

3. Taking atabrine tablets both for the prevention and treatment of malaria destroyed the testicles (five cases).

4. Testicles wasted away from disuse because there was no female companionship available at their overseas base or avoidance of sexual relations because of fear of acquiring a venereal disease (four cases).

5. Guilt complex because of illicit sexual relations while stationed overseas (four cases).

6. Toxic degeneration of the testicles due to excessive alcohol imbibition while overseas (three cases).

7. Extreme state of nervousness during missions and other hazardous situations associated with combat duty (two cases).

8. Atrophy of testicles produced by injurious sun and cosmic rays found only at high altitudes (two cases).

9. Guilt complex because of having acquired a venereal disease while stationed overseas (two cases).

10. Pressure necrosis of the testicles brought about by wearing a parachute harness which fitted snugly in the crotch (one case).

11. Deterioration of testicles brought about by the extreme heat while on tropical service (one case).

12. Deterioration of testicles brought about by the extreme cold during missions in the winter (one case).

13. Malaria caused testicular atrophy (one case).

14. Dysentery caused testicular atrophy (one case).

15. Religious complex. This man had promised God that he would never resort to any secular pleasures (in which he had listed sexual relations) if he should ever return safely from combat duty (one case).

It soon became obvious that these patients presented problems requiring psychotherapy. Many medical writings emphasize the organic aspect of this condition. In my experience, this approach has tended to avoid the basic issue, namely, that im-

potence is a symptom of aberrant functional or organic changes and not a disease *per se*. In cases of functional etiology, a prolonged course of endocrine therapy, oral medication, urethral instrumentation, and prostatic massages, when these are prescribed as specific treatment, may serve to substantiate the first impression of the patient, namely, that the structural elements of his virility have suffered a deterioration. Such therapeutic extremism is facetiously exemplified by Crookshank who writes about the response of a physician to a woman who was crying. A diagnosis of "paroxysmal lacrimation" was made and a host of antiseptic solutions, mydriatics, and dietary restrictions were prescribed. Should these measures fail, surgical removal of the tear glands was suggested.

At the same time, it was realized that the guilt would be no lighter to adopt the other extreme and regard all cases of impotence in combat returnees as being of functional etiology. No doubt was ever entertained but that functional and organic elements contributed simultaneously to many of the cases. In this connection, we never regarded ourselves as adequately competent to determine which came first.

Menninger offers some elucidation on impotence by suggesting that the inhibition of sexual function and pleasure is another form of functional focal suicide elicited by an unconscious attempt to solve unconscious emotional conflicts.

This concept has constituted the premise upon which the following treatment has been based.

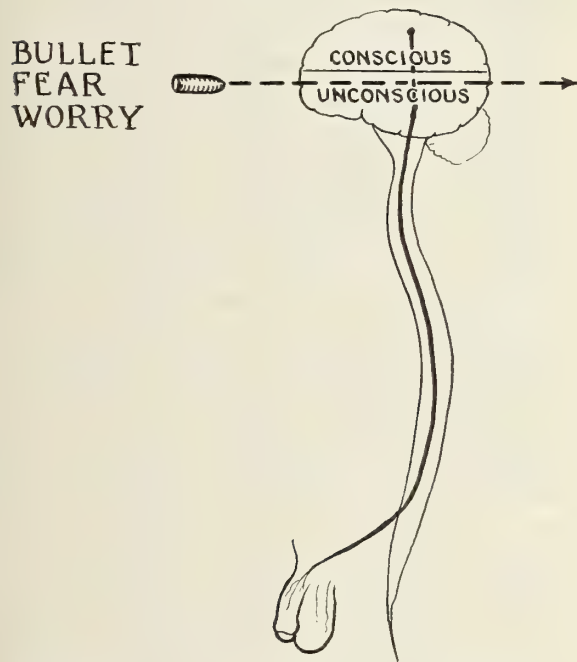
The first step in the treatment has been to encourage the patient to discuss at full length his familial, social, and educational background. He is then asked to advance any theories that he might have as to the causative factors responsible for his impotency. The essential factors gleaned from this conversation are reviewed and an attempt is made to explain the significance or fallacy of the data point by point. Wherever possible, sketches are drawn to simplify the presentation.

Medical terminology and discourses on



the various schools of psychologic thought were completely avoided. Some of the points contained in the discussion with the patients were of unproved scientific substantiation. Nevertheless, this approach enhanced the simplification of the discussion as well as the ease of comprehension on the part of the patient.

For example, a favorite diagram has been a sketch of the brain and spinal cord showing nerves running to the penis which are responsible for making an erection possible.



The brain is then divided into an upper and lower half, the former labeled conscious mind or desire and the latter labeled unconscious mind or unconscious desire. The patient is then told that so long as the unconscious mind rebels against sexual relations, the circuit is broken between the conscious desires and those nerves responsible for potency. This is further exemplified by stating that doubt as well as fears can cloud the unconscious desires and thereby produce impotence. By bringing to light all the doubts and fears which inhabit the unconscious mind, the latter is purged of the inhibiting factors responsible for his potency. The final issue is therefore not whether he is capable of the sex act but whether he desires to have sexual relations at the time.

A favorite, even if quasi-scientific, explanation of the fallacy of the concept of testicular atrophy due to oxygen deprivation or various drugs or environmental factors should be put forth as follows:

"The more complex an organ and the more important it is for the maintenance of life, the more does it require a perfect environment such as oxygen, sufficient food, and absence of injurious chemicals to survive. For example, the brain is more complex than the testicles; you can exist perfectly well without testicles but, of course, not without your brain. Therefore, the brain requires more oxygen to remain intact than the testicles (or the brain is more susceptible to the injurious effects of atabrine than the testicles, etc.). It is therefore reasonable to deduce that if the oxygen concentration, which occurred in high altitude missions, was so low as to cause destruction of your testicles, then your brain would surely have broken down before the former had occurred. You would be dead now." (The same line of reasoning would be applied to the deleterious effects of inadequate diets, cosmic rays, disease, and other environmental factors.)

Atrophy of disuse would be explained away by emphasizing the autonomic function of the testicles regardless of sexual activity. Thus, "The testicles do not degenerate from lack of sexual activity any more than do the eyes waste away from failure to read."

One of the proofs offered as evidence that testicular degeneration had not occurred would be presented in this vein. "The testicles do not have for their exclusive purpose to permit you to have an erection at will. Among other things, they are responsible for your masculine characteristics. The fact that you must shave at least every other day, that your voice is easily identified as a male one, that your breasts have not enlarged, and that you do not walk or gesture like a woman is substantial evidence to prove that your testicles are still on the job."

When urologic treatment was adminis-

tered, an attempt was made to impress the patient with the fact that the treatment was supportive and not specific. The patient would be told that the treatment was designed "to start the ball rolling"; thereafter, he would be on his own. An analogy would be drawn to the case of a man who has been ill in bed for a long time and is relearning how to walk. As this man regains his footing, the lending hand is withdrawn.

The average duration of treatment was ten weeks, the range being from three to twenty-four weekly sessions.

#### RESULTS

There were three failures in this series of patients. According to the reasons named by these men for their impotence, they were as follows:

1. Guilt complex because of illicit sexual relations while stationed overseas.
2. Extreme state of nervousness during missions and other hazardous situations associated with combat duty.
3. Religious complex.

Nineteen of this group enjoyed a return of their potency. To the best of my knowledge, there was no recurrence of their previous complaint.

#### CONCLUSION

Impotence poses a psychosomatic problem which falls partially within the province of responsibility of the urologist. Impotence should be regarded as a symptom rather than a syndrome or disease. Resorting to various endocrine preparations, central nervous system stimulants, and posterior urethral instillations has afforded us results which leave much to be desired. Psychotherapy is the privilege and obligation of all medical practitioners. One might follow the course of least resistance and refer the patient to a psychiatrist without further ado. To the physician who undertakes the task of treating a case of impotence, the promise for a satisfactory result is an eternally grateful patient. But of greater consequence is the fact that the urologist establishes himself as a specialist whose professional horizon is not obscured by a chromium-plated therapeutic armamentarium.

## RAPID POSTOPERATIVE MOBILIZATION

VINCENT D'INGIANNI, M. D.  
NEW ORLEANS

Rapid postoperative mobilization is no longer looked upon as a radical trend in surgery, and the prejudice against its exponents is beginning to disappear. It has been 48 years since Ries<sup>1</sup> mentioned his practice with early mobilization in his treatise. Since then the two most outstanding figures in this field have been Leithauser<sup>2</sup> of Detroit and Zava<sup>3</sup> in Australia.

Ever-increasing numbers of reports, both in this country and abroad, are eulogizing this form of postoperative treatment. The surgeons of World War II saw the necessities of war make ambulatory patients of thousands who would have been kept in bed had they been at home. These doctors who saw their patients rise early with no ill effects, have returned to civilian practice enthusiastic supporters of rapid mobilization. The laity as well as members of the profession are showing interest by asking questions. Popular magazines are running feature articles in lay terms entitled: *Get Up and Get Well*, *Get Out Of Bed*, *Bed May Be Bad For You*. There is a great deal of talk about this subject. Is it much ado about nothing? Let us reexamine the facts so that we may be better prepared to pass judgment on this so-called new trend in convalescence.

In order to discuss this subject it is necessary to understand the altered physiology brought about by prolonged immobilization after operation. In other words, what takes place when a patient remains at complete rest in bed for several days after operation?

One noteworthy change in physiology which is a frequent finding after operation can be classified as a respiratory complication—the inability properly to aerate the lungs. Due to the limitation of motion while reclining, there is necessarily insufficient expansion of the chest, and the inability to

\*Read before a meeting of the Orleans Parish Medical Society, April 14, 1947.



raise sputum. When the sputum thickens it acts like a plug in each bronchiole. This situation tends to diminish the vital capacity. The hemoglobin cannot be fully oxidized. Organism growth is promoted, and pneumonitis is favored.

Another physiologic change which takes place as a result of prolonged bed-rest is the diminution of the circulation in the extremities. Circulation can be quickened only by muscular contractions, which act as pumping stations of the blood. It has been shown that bicycle-like motions of the lower extremities enhance the blood flow by several hundred per cent.<sup>4</sup> Stagnant blood in the extremities promotes clots; resulting phlebothrombosis is often seen in patients confined to absolute bed rest. This occurs most frequently in those patients who have had some intima damage, especially in the veins that have been dilated from some previous disease. When phlebothrombosis or thrombophlebitis has already occurred the chances of pulmonary emboli increase.

Since muscle tone is maintained by constant use, immobilization causes atrophy and loss of tone; and circulation rate slows down accordingly.

It has been the custom to keep patients in bed until the eighth or tenth day after operation because of the "unhealed wound." However, statistics<sup>5</sup> show that wound healing is not accomplished until the twelfth or fourteenth day in those wounds closed with surgical gut. Therefore, the eighth to the tenth days would seem the most dangerous time to rise, since the sutures are at their weakest and the closing is usually not yet accomplished. To rise on the second or third day when the sutures are still strong seems more cautious to the advocates of rapid mobilization. Indeed, extensive experiments with wound healing have been carried on by Newburger.<sup>6</sup> Rats having abdominal incision were studied to determine how much pressure was required to rupture their incisions. One group was immobilized after the incisions were made; the other group was exercised on a treadmill. It was found that the incisions of the immobilized rats rupture at a much lower

pressure than those of the rats that ran the treadmill after the incisions were made. In other words, healing goes on at an excellent rate in a state of motion. As for wound disruption, it seems in no way related to mobilization, since it occurs in patients mobilized and in patients non-mobilized. It seems that there is no single cause of wound disruption, but rather that many factors play independent roles in this unpredictable phenomenon of surgery; or it may depend entirely on the individual's response to foreign material.

Before leaving this topic it can be pointed out that among the 700 cases handled by me there has not been a single case of evisceration. Nor did Leithauser,<sup>2</sup> whose cases that were early mobilized number in the thousands, report having been confronted by this complication.

The inability to create a bowel movement or to void are two usual discomforts that accompany long rest in bed. Purgation and catheterization are unpleasant and often harmful. The reclining position is conducive to ileus, causing it to linger. And so on goes the list of reasons for abandoning long bed-rest after operation.

Let us now examine the other side of the picture: the results of rapid mobilization:

When a patient sits up alongside his bed six to ten hours after an operation he necessarily exerts himself, quickens his respiration and aerates the bases of his lungs. Motion causes a cough reflex and stirs the accumulated plugs of mucous in the bronchioles, thus diminishing the chances for atelectasis or patchy pneumonitis. Turning from side to side in bed does not accomplish this as does the upright position. Distention, probably due to swallowing air, is relieved by standing.

Vital capacity can only reach its maximum when a person stands upright and moves about; it is limited by the resistance offered to the back by the bed when a reclining position is assumed. Those having upper respiratory tract infection need not fear surgery nor general anesthesia, therefore, if they rise early and attain maximum vital capacity.

Rapid mobilization quickens circulation, thus lessening the chances for stagnation, clotting, and pulmonary emboli. There have been no instances of emboli among the 700 cases upon which this report is based.

Early body motion after operation maintains muscle tone, which is highly desirable. Present day orthopedists recognize this fact; their trend is away from heavy casts which restrict motion and thus cause muscle atrophy. Motion prevents the accumulation of waste products in the tissues.

Rapidly mobilized patients do not usually need purgation or catheterization for their normal body functions are resumed early after regular motion is resumed. In a comparative study of 303 patients,<sup>7</sup> half of whom were rapidly mobilized and half of whom remained immobilized for several days postoperatively, catheterization was necessary five-tenths times per patient among the rapidly mobilized as against three times per patient among the non-mobilized.

Pain and incisional discomfort which are often intense when a patient rises on the first or second postoperative day diminishes rapidly, if one is to judge by the number of injections of narcotics needed by the patients rapidly mobilized. In the comparative study just referred to it was demonstrated that the rapidly mobilized patients averaged seven injections, whereas those who remained in bed averaged 13.

The attitudes of well-being and of independence, which are inevitable sequellae of rapid mobilization, are indeed worthy of mention.

The unanimous approval by the patients themselves of this method of postoperative treatment is significant. Of the 700 cases that have risen early, not one patient was sorry he had done so; and not one preferred delayed rising after he had experienced rapid mobilization with previous operation. They expressed their gratitude for a short hospital stay, for the curtailment of their expenses, and for getting them back on the job again as wage earners far ahead of schedule.

As an ardent proponent of rapid postoperative mobilization, I have found no contraindications for employing this mode of treatment: any patient who is a good operative risk is also a fit subject for rapid mobilization.

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## NEW ORLEANS

## Medical and Surgical Journal

*Established 1844*

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## A CENTURY OF MEDICAL PROGRESS

Under this title the Statistical Bulletin of Metropolitan Life Insurance Company sa-

lutes the centenary of the American Medical Association. During this momentous century medical and sanitary science has made amazing progress in conserving the lives and safeguarding the health of the people. The Bulletin points out that not the least of the blessings flowing out of the marked reduction in death and disability are the social and economic benefits of fewer broken families, fewer orphans, longer life with much increased production.

Not only were our forebears subject to a generally high death rate year after year but also to the periodic ravages of cholera yellow fever, smallpox and a number of other diseases. Whereas vital statistics are very poor in the country as a whole in the early nineteenth century, figures are available for New Orleans, and certain other large cities. An example of the devastation that was often inflicted on our area is the cholera epidemic in New Orleans in 1832. There were 10,471 deaths in this single epidemic, a figure in excess of ten per cent of the entire populace. The Bulletin concludes by stating that as the American Medical Association begins its second century, the physician will be concerned more and more with the degenerative diseases rather than with the diseases of environmental origin, with the chronic diseases of later life rather than with the childhood infections, and with diseases of longer duration rather than with acute conditions. These changes bring with them a host of new and challenging problems. The medical profession will, as before, meet this challenge with ever increasing effectiveness.

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DEVELOPMENTS IN THE FIELD OF  
OCCUPATIONAL DISEASES

It is somewhat surprising to learn that the South outranks the West industrially and that there are now more industrial than agricultural workers in our area. For this reason, therefore, we are constrained to give increasingly more attention to the diseases that are of occupational origin.

The U. S. Department of Labor has listed ten major hazards of employment. These

are: (1) abnormalities of air pressure, (2) abnormalities of temperature, (3) dampness, (4) defective illumination, (5) dust, (6) infection, (7) radiant energy, (8) repeated motion, pressure or shock, (9) poisons, (10) dermatoses. Grey has listed three postulates which must be proved to establish a diagnosis of occupational disease, namely, exposure to a known harmful substance; the presence of clinical symptoms and objective findings resulting from contact with a specific harmful substance; and finally, confirmation by established laboratory criteria.

It was in 1911 that effective labor legislation began in the United States. It was in that year that New York and California made the reporting of occupational diseases compulsory and New Jersey made certain occupational diseases compensable. Now all the states except one have laws requiring compensation for industrial accidents. About half of them have laws requiring compensation for at least some of the industrial diseases.

In addition to Federal and State Legislation requiring employers to pay for accidents and occupational diseases, impetus has been given by a number of voluntary organizations and scientific and professional associations. In the forefront of these latter have been the National Safety Council, the American Association of Industrial Physicians and Surgeons and the American Industrial Hygiene Association. The American College of Surgeons organized its Committee on Industrial Medicine and Traumatic Surgery in 1926. This committee has done excellent work in setting minimum standards for medical services in industry, in surveying the medical departments of industrial plants and accrediting those that measure up to their standards. The Council on Industrial Health formed by the American Medical Association has had a strong influence on the continued development in industrial medicine through its Annual Congress on Industrial Health, through its exhibits and by influencing the state and

local medical societies to appoint committees and help them develop programs on industrial medicine and health. Post Graduate and undergraduate industrial medical education are also being stressed by this Council.

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### LOEFFLER'S SYNDROME

In 1913 Loeffler described a number of patients all of whom suffered from a peculiar type of pneumonia. The salient features of the condition included transient, successive, pulmonary infiltrations, with a paucity of physical organs for the most part. In certain of the patients asthma was present but the majority had no symptoms. There was a marked blood eosinophilia ranging from 10-70 per cent. In the past year or two a fuller delineation of the condition has developed. In the roentgen-ray are noted infiltrations of homogeneous density and varying size. These may be patchy or confluent. Complete resolution in a matter of two to three weeks is usual though a few linear strands may remain. There is no predilection for upper or lower lobes. Evidences of atelectasis, calcification and cavity formation are completely lacking. Because of the mildness of the condition for the most part, the pathologic lesions have only been described once or twice. Sections of lung show replacement of the normal parenchyme by fibroblasts and collagenous fibers. Large numbers of eosinophils, plasma cells, lymphocytes and giant cells are seen in the meshes. There is a periarterial inflammatory process not unlike periarteritis nodosa.

Apparently there are a number of agents capable of eliciting this syndrome. Among these are the brucella organisms and amebas but more particularly the helminths, including *Trichinella*, *Ascaris* and *Ancylostoma*. Some 26 cases were reported from Florida, and in view of the extreme frequency of helminth infestations in Louisiana that can be little doubt of its existence here.



## ORGANIZATION SECTION

The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

*An informed profession should be a wise one.*

### STATE COUNCIL ON MEDICAL, DENTAL AND PHARMACEUTICAL SERVICES

At the last meeting of the House of Delegates, on a proposal made by the Louisiana Pharmaceutical Association, it was agreed that the Louisiana State Medical Society should participate in the formation of a State Council on Medical, Dental and Pharmaceutical Services. Our president has appointed the following committee from the State Society:

Dr. Emmett L. Irwin, Chairman; Dr. O. W. Bethea, Dr. George Hauser.

Considerable progress has been made in the direction of consummating the three organizations into a functioning unit for the better understanding of problems which are of importance to the groups. Dean McCloskey of the New Orleans College of Pharmacy, Loyola University, who formulated this idea is very active in the development of the group.

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### HIGHLIGHTS OF THE AMERICAN MEDICAL MEETING IN ATLANTIC CITY, JUNE 9-13

The new officers of the Association, elected at Atlantic City, for 1947-48 are: Dr. Roscoe L. Sensenich, South Bend, Indiana, President-Elect; Dr. Thomas A. McGoldrick, Brooklyn, N. Y., Vice-President; Dr. George F. Lull, Chicago, re-elected Secretary and General Manager; Dr. Josiah J. Moore, Chicago, re-elected Treasurer; Dr. R. W. Fouts, Omaha, Nebraska, re-elected Speaker of the House; Dr. Francis F. Borzell, Philadelphia, Vice-Speaker of the House; Dr. Dwight H. Murray, Napa, Cal., re-elected to a five year term, Board of Trustees; Dr. Edward J. McCormick, Toledo, Ohio, elected to serve a five year term, Board of Trustees.

Also: Dr. Lloyd Noland, Fairfield, Ala., re-elected as a member of the Judicial Council; Dr. John H. Musser, New Orleans, re-elected as a member of the Council on Medical Education and Hospitals; Dr. William Middleton, Madison, Wis., elected member of the Council on Medical Education and Hospitals; Drs. Stanley P. Reimann, Philadelphia and L. B. Jackson, San Antonio, elected to the Council of Scientific Assembly; Dr. James R. McVay, Kansas City, Mo., re-elected a member of the Council on Medical Service, and Drs. Elmer Hess, Erie, Pa. and Jesse D. Hamer, Phoenix, Ariz., elected to the same Council.

The House of Delegates selected Chicago as the 1948 convention city; Atlantic City for the session in 1949 and San Francisco in 1950.

Adopted in toto were the recommendations made by Dr. Edward L. Bortz of Philadelphia, our new president. They were:

1. A two-day scientific session for general practitioners at the time of the House of Delegates.

2. Change of meeting place for the semi-annual session—to convene in a different geographic district each year—at which time the two-day session for general practitioners would be held.

3. Closer affiliation with third and fourth year medical students—possibly by affiliate membership—and re-establishment of a student section in The Journal, and encouragement of presentation of scientific papers at county, state and even national levels; also to study the possibility of a student section of the scientific assembly.

4. The Secretary, in collaboration with the councils and bureaus, to prepare an attractively illustrated booklet describing the various activities carried on by the Association for distribution to graduating medical classes (Note: This booklet has been in preparation and was side-tracked

by work of the Centennial Session).

5. Further clarification of public relations activities of the Association.

6. More experienced representatives as speakers for lay groups and legislative bodies, and the establishment of a speakers' bureau to assist those representatives.

7. Greater utilization of the Woman's Auxiliary as an instrument in the field of public relations.

8. Establishment by the House of Delegates of a Committee on Nursing Problems.

9. Better channeling of information to the House of Delegates of the activities of departments, bureaus and councils.

10. Active cooperation by the Association with governmental officials to work out a program for prompt medical service in case of another national emergency.

11. The House of Delegates to take under advisement a future building program for the Association headquarters.

The Council on Medical Education and Hospitals adopted new standards for residencies and fellowships in the specialties. These will appear in the proceedings of the House to be published in *The Journal*, and will also be reprinted and distributed.

The National Conference of County Medical Society Officers billed as a "Grass Roots Conference," held its initial meeting in Atlantic City and was unanimously voted continuance. This action was approved by the House. Future meetings will be held for the purpose of developing a working partnership between the A. M. A. and every physician.

The Atlantic City registration totaled 15,667 physicians, making our Centennial Session the greatest medical meeting ever held anywhere in the world.

In keeping with the progress made at the Atlantic City Conference of County Medical Society Officers, it is felt that the plans and constructive suggestions should be carried to every state and properly presented to the various secretaries of our parish societies.

There is going to be held a regional meeting of the American Medical Association in New Orleans on October 23 and 24 this

year. The object of this meeting will be to discuss questions on medical service and public relations. It would therefore seem obvious that it might be desirable to hold a meeting of the various parish secretaries just preceding this regional meeting or else to postpone the time until just previous to the next annual meeting of the State Society. The object of this meeting would be to bring in direct contact the secretaries of our parish societies with the officers and members of various committees of the American Medical Association. At this time there could be discussed problems of mutual interest and thus get the opportunity to help implement the policies developed by the American Medical Association in relation to medical service expansion, medical care, public relations, and other vital subjects.

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#### THE AMERICAN ACADEMY OF GENERAL PRACTICE

At the American Medical Association meeting in Atlantic City there was consummated a plan to establish the American Academy of General Practice. The members of this academy would be composed of general practitioners. It would have standards and requirements for individual physicians to become diplomats and to practice general medicine under such a specialization. The initial meeting was very flattering, being attended by some 219 general practitioners. Unquestionably this is a distinct step forward and will serve to give the general practitioner a proper standing in the medical world. Our state was very fortunate in having Dr. J. P. Sanders of Shreveport placed on the board of directors. You will unquestionably receive from him appropriate information and instructions as how to how one may proceed to align himself with this progressive group of doctors. We feel assured that if the doctors so engaged will manifest their interest and enthusiasm, there can be developed in this state a very strong lever for the proper recognition of the general practice of medicine. Do give Dr. Sanders and the American Academy of General Practice your support.



# TRANSACTIONS OF ORLEANS PARISH MEDICAL SOCIETY

- August 12. Orleans Parish Radiological Society, 7:30 p. m.
- August 15. Lakeshore Hospital Staff, 8 p. m.
- August 18. Hotel Dieu Staff, 8 p. m.
- August 20. General Practitioners, Hutchinson Memorial Auditorium, 8 p. m.
- August 21. Clinico-pathologic Conference, Touro Infirmary, 12 noon.  
Veterans Administration Hospital Staff, 8 p. m.
- August 25. Board of Directors, Orleans Parish Medical Society, 8 p. m.
- August 27. French Hospital Staff, 8 p. m.
- August 28. DePaul Sanitarium Staff, 8 p. m.
- August 29. New Orleans Dispensary for Women and Children Staff, 8 p. m.
- September 3. Mercy Hospital Staff, 8 p. m.
- September 4. Clinico-pathologic Conference, Touro Infirmary, 12 noon.  
Executive Committee, Baptist Hospital, 8 p. m.
- September 5. Ochsner Clinic Staff, 8 p. m.  
N. J. TESSITORE, M. D., Secretary.

## NEWS ITEMS

Dr. James W. Burks, Jr., addressed the West Tennessee Medical and Surgical Association at Dyersburg on May 22. He spoke on "Some Common Epidermal Sensitizations."

Dr. Wm. B. Clark was elected to membership in the American Ophthalmological Society at the meeting of this organization at Warm Springs, Va., June 5-7.

Dr. Clark served by invitation as an Associate Examiner on the American Board of Ophthalmology examinations which were given at Philadelphia, June 15-18.

Dr. J. W. Davenport, Jr., and Dr. Edwin H. Lawson attended a meeting of the South Mississippi Medical Society and the South Mississippi Medical Society Auxiliary at Hattiesburg, June 12.

Dr. Davenport presented a paper entitled, "A Practical Approach to the Rh Problem"; Dr. Lawson spoke on "Meningitis Due to Salmonella."

Dr. Daniel J. Silverman read a paper prepared by himself and Dr. Alan Leslie, on "Salmonella—A Cause of Chronic Bacteria Dysentery" at the meeting of the American Gastro-Enterological Association in Atlantic City immediately preceding the AMA Convention.

Dr. Early Conway Smith was recently re-elected president of the Lakeshore Hospital Staff. Other officers re-elected were: Dr. Robert M. Willough-

by, vice-president; and Dr. Alan Leslie, secretary-treasurer.

Members of the executive committee for the coming year are: Drs. Willoughby, E. D. Matthews, L. J. O'Neil, W. P. Bradburn, Jr., Irven Cahen, Edward W. Nelson, John S. Herring, Wm. C. Rivensbark, and H. L. Kearney.

## CHANGES IN MEMBERSHIP ROLLS

During the month—

Five active members, Drs. Harry Fishbein, Allan J. Hill, Emile Maltry and Paul B. Reaser, and one intern member, Dr. A. S. Warren resigned because of removal from New Orleans.

Four members passed away, Dr. Theobald R. Rudolf, active; Drs. W. W. Calhoun, E. D. Friedrichs and J. A. Lewis, inactive.

The following members participated in the scientific program of the A. M. A. at the meeting in Atlantic City June 9-13:

Dr. John Adriani opened the discussion on Drs. J. J. Jacoby, J. M. Coon and H. M. Livingstone's paper—"Effect of Procaine on Liver Function: An Experimental and Clinical Study."

Dr. Ruth G. Aleman opened the discussion on Drs. Jerome L. Kohn and Alfred E. Fischer's paper—"Management of Whooping Cough in Infants."

Dr. W. D. Beacham presented a paper on "Ectopic Pregnancy."

Drs. George E. Burch and Clarence T. Ray presented a paper on "The Cardiovascular System as the Effector Organ in Psychosomatic Phenomena."

Dr. Burch participated in the Question and Answer Conference on Cardiovascular Diseases, discussing the "Problems in Electrocardiography."

Dr. Ansel M. Caine opened the discussion on Dr. John B. Dillon's paper—"Anesthesia in the Aged."

Drs. Manuel M. Garcia and Leon J. Menville presented a paper on "Critical Evaluation of Surgical and Radiation Therapy for Carcinoma of the Cervix."

Dr. George M. Haik presented a paper on "Intraocular Foreign Bodies: Wartime Experiences Applied to a Peacetime Problem."

Dr. James K. Howles and Dr. E. R. Gross of Philadelphia presented a paper on "Oral Bismuth Therapy in Syphilis and Various Inflammatory Dermatoses."

Dr. Mercer G. Lynch presented a paper on "Traumatic Injuries of the Larynx, Especially Gunshot Wounds and Their Repair."

Dr. Champ Lyons presented a paper on "Management of Protein Deficiency in Surgical Patients: Use of Whole Blood Transfusion."

Dr. Alton Ochsner, chairman of the Section on Surgery (General and Abdominal) gave the chairman's address: "Carcinoma of the Lung."

Dr. William Parson opened the discussion on Dr. Sidney C. Madden's paper on—"Protein Nitrogen Following Injury."

Drs. Ralph V. Platou, John Kometani and Norman Woody presented a paper on "Pediatric Deaths in a Large Central Hospital."

Dr. M. T. Van Studdiford opened the discussion to Drs. G. H. Faget and Paul T. Erickson's paper—"The Chemotherapy of Leprosy."

*Scientific exhibits were presented by—*

Drs. George E. Burch and Clarence T. Ray—"Cardiovascular Syphilis."

Drs. George E. Burch and Paul Reaser—"Radio Elements and Mechanism of Congestive Heart Failure Radiosodium."

Dr. Grace A. Goldsmith—"Treatment of Macrocytic Anemia with Pteroylglutamic Acid."

Drs. Champ Lyons, H. S. Mayerson and Paul T.

DeCamp—"Chronic Shock, the Problem of Reduced Blood Volume in the Chronically Ill Patient."

Dr. J. Brown Farrior—"Ear Surgery."

Dr. James K. Howles, DeW. F. Mullins and William B. Stewart—"Cutaneous Gramulomas."

Drs. John Adriani and David A. Davis—"Physiologic Changes During Spinal Anesthesia."

*Awards—*

Drs. George E. Burch and Paul Reaser received the GOLD MEDAL in group one for their scientific exhibit on "Radio Elements and Mechanism of Congestive Heart Failure Radiosodium."

Drs. Champ Lyons, H. S. Mayerson and Paul T. DeCamp received a CERTIFICATE OF MERIT in group one for their scientific exhibit on "Chronic Shock, the Problem of Reduced Blood Volume in the Chronically Ill Patient."

## LOUISIANA STATE MEDICAL SOCIETY NEWS

### C A L E N D A R

#### PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

#### LOUISIANA STATE MEDICAL SOCIETY ANNUAL MEETING

The Ouachita Parish Medical Society, in cooperation with the Executive Committee of the State Society, has selected April 12, 13, and 14, 1948, for their annual meeting dates. Plans are being developed to assure our profession a most entertaining, educational and progressive meeting.

#### SNELLING CHAIRMAN OF ARRANGEMENTS COMMITTEE

Dr. John G. Snelling, Jr., has been appointed chairman of the Arrangements Committee when the Louisiana State Medical Society meets in Monroe next year. The meeting will be held the second week in April, beginning on the twelfth and ending on the fourteenth.

#### AMERICAN ACADEMY OF GENERAL PRACTICE

The following Associated Press dispatch appeared in the N. O. Times-Picayune. It was felt that it should be reproduced in full as it recounts

a very important development in the field of general practice.

#### GENERAL DOCTORS ORGANIZE SOCIETY LOUISIANA FIRST TO COMPLETE STATE ACADEMY GROUP

Alexandria, La., July 13.—Approximately 100 doctors from all parts of Louisiana today organized a Louisiana state branch of the new American Academy of General Practice which was formed on a nationwide basis at the Atlantic City meeting last June 10 of the American Medical Association.

The American Academy of General Practice is expected to fulfill, among general practitioners, the same functions as are performed for surgeons by the American Academy of Surgeons and for physicians by the American Academy of Physicians. Its object is to revise the standards of general practice and bring greater recognition of the general practitioner.

#### First Statewide Group

The action today made Louisiana the first state in the nation to complete statewide organization. The new organization was pictured by speakers at the all day meeting as potentially destined to be, on a nationwide basis, the most powerful of all



medical organizations within the American Medical Association, because 60 per cent of the country's doctors are general practitioners.

The Louisiana organization elected Dr. J. P. Saunders of Shreveport president. Under the by-laws and constitution adopted, there is also a post of president-elect who will become president a year hence. This went to Dr. Guy Jones of Lockport. Dr. D. B. Barber of Alexandria was elected vice-president and Dr. J. W. Atkinson of New Orleans, treasurer.

The first board of directors, one from each congressional district in the state, is made up of the following:

First District, Dr. Nicholas J. Chetta, New Orleans; Second District, Dr. J. B. Gray, New Orleans; Third District, Dr. Philip Robichaux, Raceland; Fourth District, Dr. S. L. Gill, Shreveport; Fifth District, Dr. E. L. Carroll of Columbia; Sixth District, Dr. M. C. Wigginton, Hammond; Seventh District, Dr. O. W. Topp, Oberlin; Eighth District, Dr. H. P. Forsythe, Alexandria.

#### ADDITIONAL ATTENDANCE AT THE A. M. A. MEETING

It was noted in an editorial last month that the final figures for attendance at the A. M. A. meeting were not available at the end of the scientific meeting. This is responsible for our unfortunate neglect to publish the fact that Drs. A. A. Herold, J. P. Sanders and Joseph Shavin, of Shreveport, were all in attendance at the meeting.

If the Journal missed any other Louisiana men it would be glad to name them in an approaching number.

#### CHARITY HOSPITAL

A meeting of the Medical Division of Charity Hospital was held on Tuesday, June 17 in the Auditorium of the hospital. The program consisted of the following: miliary tuberculosis: response to streptomycin therapy, by Dr. Philip B. Johnson, and bacterial endocarditis: two cases requiring massive antibiotic therapy, by Drs. Norman S. Gilbert and Carl Gulotta.

#### TOURO INFIRMARY

The Medical Staff of Touro Infirmary has discontinued its regular monthly meeting for the summer. The meetings will be resumed in October.

#### SHAFFER TO HELP ORGANIZE MEDICAL SCHOOL

Dr. Morris Shaffer, former Rhodes Scholar and present Professor of Bacteriology at Tulane Medical School has been signally honored. He has accepted an invitation to go to Jerusalem where he will organize a Basic Science Department at the University of Jerusalem. He will also advise as to the establishment of a four year medical school.

He will remain in Palestine through the summer, returning in time to resume his duties in the Department of Bacteriology at the Tulane University School of Medicine.

#### ARMY ENGINEERS TO BUILD GREATEST MEDICAL CENTER

What is planned to be the greatest medical research center in the world will be built at Forest Glen, Maryland, by the Corps of Engineers for the Office of the Surgeon General, according to a recent announcement made by Major General Raymond W. Bliss, The Surgeon General. In keeping with technological advances in all fields, based on experiences in the late war, the center will be equipped to anticipate and meet the medical problems of the future as well as to cope with those of the present. The initial cost is estimated at approximately \$40,000,000. Construction will be supervised by the District Engineer, Washington, D. C. Engineer District.

Officially designated as the "Army Medical Research and Graduate Teaching Center," the project will consist of a 1,000-bed general hospital, capable of expansion to 1,500 beds; the Army Institute of Pathology building; the Army Medical Museum and Center Administration building; Central Laboratory Group buildings; and the Army Institute of Medicine and Surgery. A working library, animal farm, quarters for the staff and other buildings are included in the plans.

Located just outside of Washington, the new Army Medical Center will have the advantage of close relationship to the Walter Reed General Hospital, the Naval Medical Center, the medical schools of the District and the proposed new Washington Medical Center, with all of whom ideas can be interchanged.

#### NEW ORLEANS GYNECOLOGICAL AND OBSTETRICAL SOCIETY

At a recent meeting of the New Orleans Gynecological and Obstetrical Society, Dr. Earl Conway Smith was elected president of the organization; Dr. W. D. Beacham was named president-elect; Dr. Curtis H. Tyrone was selected as vice-president; Dr. John S. Herring as secretary and Dr. Harry Meyer treasurer.

#### EMIC TO END

On July 1 liquidation began of the Louisiana Emergency Maternity and Infant Care program which was administered by the maternal and child health section of the state health department. Payments will be made to physicians and hospitals for maternity or infant care which was authorized before July 1, 1947. Maternity cases where pregnancy began prior to July 1, 1947; infants under one year of age during the period July 1, 1947 to June 30, 1948, and infants born to mothers who

were pregnant before July 1, 1947, will be eligible for medical and hospital care paid for through EMIC funds during the next two fiscal years.

Approximately 25,000 mothers and babies received care through the program, which began December 1, 1943, at a cost of more than \$1,652,389.

In announcing the liquidation, Dr. Waldo Treuting said "The Louisiana state health department would like to express its appreciation to all physicians, hospitals, social agencies and other groups who have cooperated in making this EMIC program meet the needs of the wives and infants of Louisiana service men and women."

#### MEDICAL PUBLICATIONS NEEDED OVERSEAS

As a result of war and persecution, doctors, dentists and technicians in allied fields throughout Europe have been deprived for more than ten years of news of the latest developments in their professions—the kind of news and analysis contained in this journal.

When you have finished this issue, put it to work by sending it to the SOS (Supplies for Overseas Survivors) Collection of the Joint Distribution Committee, 1 West 39th Street, New York 18, N. Y. It will be placed in a library in a D. P. camp, child care center, hospital or school, for use by professionals desperately anxious to bring themselves up-to-date on the knowledge forcibly kept from them by the Nazis.

#### INSTRUCTIONAL COURSE IN ALLERGY

The American College of Allergists has announced that its annual Fall Graduate Instructional Course in Allergy will be given in Cincinnati, Ohio, November 3-8, inclusive, under the auspices of the Medical College of the University of Cincinnati.

The program this year is the best ever offered by the College. Forty-six formal lectures are listed and also a special allergy clinic of case presentations. An added feature this year will be three informal discussion groups led by various members of the faculty.

Programs and complete information can be obtained by writing to the College Secretary, Dr. Fred W. Wittich, 423 La Salle Medical Building, Minneapolis 2, Minnesota.

#### AMERICAN COLLEGE OF SURGEONS

The thirty-third annual clinical congress of the American College of Surgeons will be held at the Waldorf-Astoria, New York, September 8-12. A variety of clinical and scientific features have been provided by Dr. Howard A. Patterson, of New York, Chairman of the Committee on Arrangements, and his committee.

On the first day Dr. Irvin Abell will inaugurate President-elect Dr. Arthur W. Allen, of Boston,

and the other new officers.

At this time Dr. Abell will give the address of the retiring president, speaking on the subject "The Spirit of Surgery." Dr. Allen O. Whipple, of New York, will deliver the Martin Memorial Lecture.

The convocation, at which time nearly six hundred initiates will be made fellows, is to be held on Friday evening, September 12. Dr. A. C. Ivy, of Chicago, will give the fellowship address.

#### NEW BUILDING FOR ALOE COMPANY

The A. S. Aloe Company gave a buffet luncheon and cocktail party for the medical men of New Orleans and vicinity when they opened their beautiful new building at 1425 Tulane Avenue. The building was officially opened by Mayor Morrison and Howard F. Baer of the Aloe Company.

The building is located directly opposite from Charity Hospital and has an enormous stock. This stock is not only for the purpose of supplying the medical profession of the far South but also the physicians of Latin America. A beautiful feature of this new building will be a mural picturing seven eras of Louisiana Medical History. This will be painted by Franklin Boggs, a noted war muralist.

#### INTERNATIONAL COLLEGE OF SURGEONS

The International College of Surgeons, United States Chapter, will hold its Twelfth Annual Assembly and Convocation in Chicago, September 28-October 4, 1947.

The program will include operative and non-operative clinics, demonstrations, symposia, forums, medical motion pictures, exhibits and the formal dedication of the new library and permanent home of the United States Chapter. All meetings, with the exception of the operative clinics, will be held in the Palmer House and the Stevens Hotel.

#### POST GRADUATE COURSE IN INFECTIOUS DISEASE

The Emory University School of Medicine announces a post graduate course in infectious diseases to be conducted in cooperation with the Georgia Department of Public Health. It will be held September 18-19, 1947, at the Grady Memorial Hospital, Atlanta, Ga.

This course is planned specifically for the public health physician and general practitioner. It is intended to be a practical and comprehensive study of the latest methods of clinical and laboratory diagnosis and treatment of communicable diseases, including venereal infections.

#### THE AMERICAN CONGRESS OF PHYSICAL MEDICINE

As previously announced this organization will hold its twenty-fifth annual scientific and clinical session September 2-6 inclusive, at the Hotel Radis-



son, Minneapolis. In addition to the scientific sessions, the annual instruction courses will be held September 2-5. These courses will be open to physicians and the therapists registered with the American Registry of Physical Therapy Technicians. For information concerning the convention and the instruction course, address the American Congress of Physical Medicine, 30 North Michigan Avenue, Chicago 2, Illinois.

Dr. G. H. A. Clowes, Ph. D., Sc. D., LL. D., Director Emeritus of the Lilly Research Laboratories, was honored by the American Diabetes Association at its recent annual meeting in Atlantic City, New Jersey. He delivered the annual Banting Memorial address and was awarded the Banting Medal which is given in recognition of distinguished service in the field of diabetes.

Under Dr. Clowes' direction, the Lilly Research Laboratories co-operated with the University of Toronto and Drs. Banting and Best in the early development of insulin of sufficient purity and stability to permit its widespread clinical use throughout the world.

#### DR. SCHEELE TO REPLACE DR. SPENCER

The resignation of Dr. R. R. Spencer as Chief of the National Cancer Institute of the U. S. Public Health Service to be effective July 1 was announced at the quarterly meeting of the Institute's National Advisory Council, in Bethesda. At the same time, Dr. Thomas Parran, Surgeon General, informed the Council that Dr. Leonard A. Scheele, formerly Assistant Chief of the Institute, would succeed Dr. Spencer.

Simultaneously, the appointment of Dr. A. C. Ivy, vice-president of the University of Illinois and one of the country's leading physiologists, to fill the empty post of Executive Director of the National Cancer Advisory Council was announced. Dr. Ivy succeeds Dr. George M. Smith, Professor Emeritus of Yale University, who resigned some months ago for reasons of health.

#### AMERICAN ASSOCIATION FOR THE STUDY OF GOITER

The American Association for the Study of Goiter will hold its next meeting in the King Edward Hotel, Toronto, Canada, May 6-8, 1948. The program for the three day meeting will consist of papers dealing with goiter and other diseases of the thyroid gland, dry clinics and demonstrations.

#### NEWS ITEMS

Dr. Ralph H. Riggs of Shreveport, Louisiana, has been one of fifty from a group of well over 650 applicants selected to take Dr. Samuel Fomon's course in Rhinoplasty. Dr. Fomon has been doing plastic surgery for a number of years, the last five or six years in the Manhattan General Hospital in

New York City. For some time he has been giving a course to the Board Members of the Ear, Nose and Throat Group, teaching them the basis of Rhinoplasty and Otoplasty. This course is sponsored by the American Otorhinologic Society for the Advancement of Plastic and Reconstructive Surgery.

A permanent position is open to a physician in Melville, Louisiana, St. Landry Parish. Please contact the President of the Lions Club.

#### CASH SICKNESS BENEFITS FOR RAILROAD WORKERS

A cash sickness benefit system for railroad workers will begin operating throughout the nation on July 1. All disabilities which prevent railroad employees from working, regardless of how or where they occur, are covered under the program.

A physician's statement of sickness will be required before claims can be paid. It is believed that the program will require about 650,000 medical examinations a year. Employees are free to choose their own doctors, and any physician to whom an employee goes for examination or treatment may supply the information required as initial proof of an employee's claim. The forms on which medical information will be requested from a physician are the "Statement of Sickness" and the "Supplemental Doctor's Statement."

#### BIRTHS EXCEED 1,500,000 IN FIRST FIVE MONTHS OF 1947

Births in May are estimated to have numbered 302,000 in the United States, according to figures released by the National Office of Vital Statistics, U. S. Public Health Service. This is 29 per cent more than the estimate for May of last year and it brings the total for the first five months of this year to 1,572,000.

Although the birth rate of 26.4 per 1,000 population including the armed forces overseas for the 5-month period January to May, 1947 was nearly 40 per cent higher than the provisional rate of 19.1 for the corresponding period of 1946, the birth rate has been lower this year than it was in the last four months of 1946 when it reached record breaking heights. The decrease has taken place in spite of the fact that publications of this office show that the numbers of marriages reported 10 to 12 months ago and throughout 1946 were unusually large. It is possible that the peak in the birth rate in the latter months of 1946 was due not only to first births to newly married couples, but also to births to families who already had children and first births to couples married before or during the war. The fact that the birth rate has decreased while marriages remained high suggests that now second and third births to established families and first births to persons married more than one year

are adding less to the birth rate than they did at the end of last year.

The estimated number of births in each of the 46 states reporting monthly and the District of Columbia appear in the Monthly Vital Statistics Bulletin being released by the National Office.

#### HEALTH IN NEW ORLEANS

The Bureau of Census, Department of Commerce, reported that for the week ending June 14 there occurred in the city of New Orleans 110 deaths of which 74 were in white persons and 36 were in non-white individuals. The three year median correspondingly showed a total of 139 deaths so that the area enjoyed a somewhat reduced mortality in contrast to the median. For the following week there was a total of 129 deaths, 82 of which were in white people. The week ending June 28, however, showed a marked decrease to a total of 99, 63 of whom were white, and 36 of whom were non-white. For the corresponding three year median there were 154 deaths.

#### INFECTIOUS DISEASES IN LOUISIANA

The weekly morbidity report for the State of Louisiana for the week ending May 31, showed measles leading all other reportable diseases with a total of 27 cases. Following measles, numerically, came pulmonary tuberculosis with 19 cases reported, cancer with 18, and whooping cough with 10 cases. There were no other diseases recorded in figures greater than 10. For the week ending June 14, cancer had assumed the first position with a total number of 66 cases. Of the other diseases exceeding 10 there were 45 instances of measles, 44 of unclassified pneumonia, 24 of pulmonary tuberculosis, 23 of whooping cough, and 13 of pneumococcal pneumonia. For the week ending June 21, whooping cough led with 55 cases followed by measles with 45, pulmonary tuberculosis 43, cancer 33, malaria 16, septic sore throat 14, chicken pox 14, unclassified pneumonia 11, and bacillary dysentery 10. It will be noted that there is a sharp rise in malaria during this period which however, was not continued through the week ending June 28 in which the number dropped to 3 cases. In the same interval, cancer was most prevalent of reported diseases, with 55 examples followed by pulmonary tuberculosis with 47, unclassified pneumonia 28,

amebiasis 12, and measles 11. There was but one case of polio-myelitis reported in the state.

#### MONTHLY MORBIDITY FOR VENEREAL DISEASES STATE OF LOUISIANA Month Ending May 31, 1947

	Total Month This	Total Months Previous	Total 1947 To Date
Chancroid	59	221	280
Gonorrhea	1210	5069	6279
Granuloma inguinale	25	57	82
Lymphopathia venereum	5	33	38
Syphilis	919	3989	4908

#### INFANT MORTALITY TOTAL

The mortality total for infants for the week ending June 14 was 16, equally divided among white and colored. In the following week there were 11 deaths among infants of which total 7 were white. For the week ending June 28 there was a precipitous drop to a total of 3 deaths, 2 of whom were white children.

#### JOSEPH TILFORD SCOTT, M. D.

1870-1947

One of the most prominent older physicians of New Orleans died July 5, 1947, after a relatively short illness. Dr. Scott, who was 77 years of age, had retired from a very active practice some ten years ago. He was a graduate of Tulane in the class of 1894 and for many years was connected with the U. S. Public Health Service in New Orleans. Dr. Scott had a unique genealogical record. He was related to three United States Presidents, Madison, Monroe and Taylor.

#### FRANCIS C. BENNETT, M. D.

1870-1947

Dr. Francis C. Bennett, of Monroe, died on June 27. He was a graduate of the Medical College of Kansas and had been an active member of the Louisiana State Society for many years. His interest and influence in organized medicine will be greatly missed.

## BOOK REVIEWS

*The Physico-Chemical Mechanism of Nerve Activity*: By David Nachmansohn & others. New York, Annals of the New York Academy of Sciences, 1946. Pp. 228.

This monograph embodies the lectures given at a conference held under the auspices of the New York Academy of Sciences in which the leading

investigators in the field participated. The lectures covered the most recent experiments in the field of nerve activity, synaptic transmission, and nerve metabolism. There are twelve lectures on various aspects of these fields, an introduction by Tracy J. Putnam, and a conclusion by John F. Fulton. Much of the work reported is concerned with



the question as to whether the transmission of nerve impulses is electrically or chemically mediated. The electrical hypothesis is upheld by Dr. Eccles, whereas, Nachmansohn has given in detail his reasons for believing in the chemical mediation theory. Of particular interest is the lecture by Dr. Gerard entitled "A Critique of the Role of Acetylcholine," in which he questions the importance of acetylcholine in junctional transmission in the central nervous system and suggests that the time is ripe for a new concept of nerve impulse transmission.

The monograph is recommended to those who are interested in obtaining a first hand report of the modern concept of nerve activity as given by the workers who are best equipped to present this information.

H. S. MAYERSON, PH. D

*Progress in Gynecology*: By Joe V. Meigs, M. D. and Somers H. Sturgis, M. D. New York, Grune and Stratton, 1946. Price \$7.50.

In the preface, the author states "It was our policy to select the hobby of each author and ask him or her to write how each felt about a certain subject". The wisdom of this plan is reflected throughout this capital volume which contains contributions by seventy-one authorities in the fields of gynecology and endocrinology.

The careful grouping of the contributions into ten main subdivisions: Growth and Physiology Diagnostic Methods, Functional Disorders, Interrelationship of Endocrine Glands, Sterility and Reproduction, Infections and Their Treatment, Benign Growths, Malignant Growths, Operative Technique, Preoperative and Postoperative Care, is praiseworthy.

Each subject is carefully and completely covered by a recognized authority in each field, in a clear and lucid manner. Seventy-one illustrations and charts of excellent quality, amplify the subject matter. This volume is a must for medical men, surgeons, gynecologists, and endocrinologists. It is a comprehensive, authoritative, enlightening, post graduate course for anyone.

CONRAD G. COLLINS, M. D.

*Ambulatory Proctology*: By Alfred J. Cantor. New York, Paul B. Hoeber, Inc., 1946. Pp. 524. Price \$8.00.

An excellent work, this volume with its 32 chapters covers the field of proctology (excepting colonic surgery) very thoroughly. Noteworthy are the chapters on hemorrhoids and anorectal fistula. Along with chapters on the usual subheads, there are ones on pediatric proctology, electro-surgical technic, and an excellent one on intestinal parasites.

The text is well written in a clear and pleasant style and is abundantly illustrated with good

drawings and photographs apparently selected with great care and certainly good judgment.

MAURICE LESCALE, M. D.

*X-ray Diffraction Studies in Biology and Medicine*: By Mona Spiegel-Adolf, M. D. and George C. Henny, M. S., M. D. New York, Grune and Stratton, 1947. Pp. 209, 12 tables, 86 figs.

Considerable progress has occurred in the field of x-ray diffraction and the newer technics have been employed in biologic research. The authors have collected the scattered information available, reviewed their own studies of ten years and presented them with the pertaining literature.

This volume consists of twelve chapters and indices of authors and subjects.

Chapter I pertaining to the theory of x-ray diffraction is of considerable interest. It has been shown that electrons will vibrate in the path of an x-ray beam. Radiation of the same wave length as the incident beam will be emitted by the electron. The atom scatters x-rays to an extent depending on the number of orbital electrons it contains and the arrangement or distribution of these electrons. The diffracted rays produce a pattern of spots, arcs or halos on the film. The pattern produced is an index of the molecular arrangement.

In the second chapter, apparatus and technics are discussed. The apparatus consists of: (1) a high voltage generator and x-ray diffraction tube, (2) a diaphragm system for restricting the x-ray beam to a small area, (3) a holder for the specimen, and (4) the cassette or film holder. Various types of apparatus and the various technics employed are considered rather completely.

Chapter III deals with the interpretation of diffraction patterns. Chapters IV through XII consider diffraction studies on carbohydrates; amino acids; proteins; nucleic acids and nucleoproteins; muscle; lipides; nerves; steroids; and bones, teeth and concretions, respectively.

While the text is clearly written, the brevity of the work requires careful reading for understanding. Unnecessary detailed physical and mathematical discussions have been omitted. The biologist and the research physicians will find this volume a valuable addition to the library.

J. N. ANÉ, M. D.

*Genetics, Medicine, and Man*: By H. J. Muller, C. C. Little, and Laurence H. Snyder. Ithaca, Cornell University Press, 1947. Pp. viii + 158, figs. 29. Price \$2.25.

Six lectures presented at Cornell University in 1945, in the series of Messenger Lectures on the Evolution of Civilization, are here made available to a larger public. Each of the authors is responsible for two chapters, or lectures. Muller writes on fundamentals of the genetic mechanisms, Little deals with parental influence, growth and individu-

ality, and Snyder is concerned specifically with human heredity, including the mutant gene.

The book will be welcomed by medical men. It offers first a vivid account of the nature and behavior of genes. With this background the reader proceeds understandingly into the discussion of aspects of genetics that are of immediate practical importance in medicine. In these days no one engaged in medicine can afford to ignore the contributions toward its progress that are being made in the field of genetics. The present book is a stimulating introduction to these contributions and to ways of thinking that should be cultivated.

HAROLD CUMMINS, PH.D.

*The Head, Neck and Trunk:* By Daniel P. Quiring. Philadelphia, Lea & Febiger, 1947. Pp. 115, frontispiece, figs. 103. Price \$2.75.

This volume on muscles of the head, neck and trunk follows the plan of the author's "Extremities," published in 1945. Excepting a few instances in which two or more muscles are shown, each figure is devoted to the illustration of a single muscle, with its nerve supply and blood supply. These structures are overlaid on outlines of the neighboring skeletal framework, so as to represent their relations to it and the attachments of the muscle. Motor points of the head and neck are illustrated in the final figure. The text accompanying each figure is a concise statement of origin, insertion, function, nerve supply and blood supply

—concluded with page references to two of the standard textbooks of gross anatomy.

HAROLD CUMMINS, PH. D.

#### PUBLICATIONS RECEIVED

Charles C. Thomas, Springfield, Illinois: *Cineplasty*, by Henry K. Kessler, M. D., Ph. D.; *Diseases Transmitted from Animals to Man* (3rd Edition), by Thomas G. Hull, Ph. D.; *Osteotomy of the Long Bones*, by Henry Milch, M. D.

Chemical Publishing Co., Brooklyn: *Practical Emulsions*, by H. Bennett.

Grune & Stratton, New York: *Dermatologic Clues to Internal Disease*, by Howard T. Behrman, M. D.; *Diagnosis and Treatment of Diarrheal Diseases*, by William Z. Fradkin, A. B., M. D.; *Paravertebral Block in Diagnosis, Prognosis, and Therapy*, by Felix Mandl, M. D., F.I.C.S.

Lea & Febiger, Philadelphia: *Occupational Diseases of the Skin*, by Louis Schwartz, M. D., Louis Tulipan, M. D., and Samuel M. Peck, B. S., M. D.; *A Manual of Fractures and Dislocations*, by Barbara Bartlett Stimson, A. B., M. D., Med. Sc. D., F.A.C.S. *A Manual of Otology, Rhinology and Laryngology*, by Howard Charles Ballenger, M. D., F.A.C.S.; *Roentgen Interpretation*, by George W. Holmes, M. D., and Laurence L. Robbins, M. D.

Williams & Wilkins Company, Baltimore: *Histopathology of the Ear, Nose and Throat*, by Andrew A. Eggston, B. D., M. D., and Dorothy Wolff, A. B., M. A., Ph. D.



# New Orleans Medical

and

## Surgical Journal

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No. 3

### THE PRESENT DAY TREATMENT OF MALARIA\*

A. J. WALKER, M. D.  
NEW ORLEANS

In the vast majority of cases, if the patient's symptoms are due to malaria, the parasite can be demonstrated in an adequately stained thick blood film. In highly endemic areas, possibly one patient in two hundred will be encountered in which the acute symptoms will demand immediate treatment even before a blood examination can be made. Efforts to make a diagnosis should be continued even after treatment has begun. "Fever with negative smears should be studied, not treated. There is no need to hurry."<sup>1</sup> At the same time, a careful physical examination may reveal the presence of a pneumonia, meningitis or other condition which makes the malaria infection one of secondary importance.

Falciparum malaria can be fatal but it is also more readily cured. Some forms of malaria show great tendency to relapse while other infections are, at times, self limited.

Specific treatment includes: (1) management of the presenting attack; (2) eradication of the infection if possible; (3) suppression of further clinical manifestations; (4) prevention of new infections developing to clinical proportions.

If one analyzes the situation of a patient

in whose blood the finding of some thirty definite parasites has permitted a diagnosis of vivax malaria to be made, we are struck by the fact that, aside from knowing the existence of the infection and its specific name, we know extraordinarily little. There are three variables on which the course of the disease and the success of any form of treatment depend:

<i>Species</i> strain variations	<i>Drug</i> varied behavior	<i>Individual</i> resistance susceptibility suppression
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Because of these variables, the League of Nations Commission, in 1933, was unable to recommend any standard form of treatment.<sup>10</sup> Such variables also explain why a treatment method seemingly highly effective in one region may prove quite disappointing with the same species in a different part of the world. Examples: varying relapse rates in vivax infections; a few atabrine-resistant strains of falciparum on Wewak.<sup>2</sup>

The place which quinine has occupied in malaria therapy for over a century has now been preempted by atabrine and other synthetic compounds known to be definitely superior to quinine when administered in adequate dosages. This time-honored and expensive drug is, therefore, relegated to the position of adjuvant to certain other substances.

Over the years, the scheme of dosage for quinine was developed empirically and that used for the individual attack is essentially the same as used thirty years ago. At the

\*Read before the Sixty-seventh Annual Meeting of the Louisiana State Medical Society, New Orleans May 14, 1947.

Adapted from the section on Malaria in Communicable Diseases, by R. L. Pullen—in press.

time plasmochin was developed, in 1926, the medical world was quite ready to try out other compounds. Unfortunately, this very excellent antimalaria drug was found to be toxic in certain instances and its use came to be limited to its gametocidal action. In a few years the profession became extremely cautious of it. This caution was carried over to all other synthetic drugs and actually hindered a really thorough clinical trial of the next synthetic to appear in 1930—atabrine.

Still working somewhat empirically in regard to dosage, atabrine was given in as small doses as possible. The original treatment was 0.1 gm. thrice daily for five days, later increased to seven days. Even on a five day treatment some patients became yellow, since atabrine is a yellow acridine dye with predilection for the skin. This yellow color suggested to the laity and too often to the physician—jaundice—and therefore liver damage, neither of which was present nor can be produced by atabrine. Furthermore, it was noted, quite correctly, that atabrine did not seem to bring about clinical improvement as quickly as did quinine.

Before further new drugs against malaria were forthcoming, the era of the sulfa group of drugs arrived. The early recognition that their efficacy depended upon adequate blood concentrations soon led to comparatively simple methods of determination of sulfa blood levels. It was not long before the same principles were applied to atabrine. During experiments which showed that the fears of atabrine toxicity were groundless, it was also seen that adequate blood concentrations were not obtained with the old regime until about the fifth day.<sup>3</sup> Ninety per cent of the atabrine is fixed in the tissues before the blood concentration begins to build up. Quinine, on the other hand, is rapidly absorbed and its maximum concentration is reached in four hours. When the obvious was tried, namely to "load" the atabrine dosage in the first 24 hours, it was soon apparent that atabrine was equally or more effective than quinine and the required dosage was readily toler-

ated. The feared toxicity had proved to be a myth born of skepticism and conservatism.

In 1939, the Germans patented a drug called "sontochin" which, for some reason, was not given an adequate clinical trial until brought to America in 1942. Another drug of this same series was "resoquin" or what we know as chloroquine.<sup>5</sup> This white substance has roughly the same therapeutic properties as atabrine, is effective in fewer doses and does not have the objectionable yellow color.

Quinine and its equivalent-totaquine, atabrine and chloroquine complete the list of those drugs which have proved to be effective in removing the asexual forms of the parasite from the blood and relieving the clinical symptoms. Since they are capable of doing only this, the futility of long continued treatment was soon evident. Moreover, after cessation of these drugs given suppressively, further clinical activity occurred. One very important finding from the investigations of effects of atabrine suppressive therapy came to light.<sup>4</sup> If continued for 23 days after the infective bite, falciparum infections could be acquired, could reach demonstrable, if not clinical proportions and be completely eradicated. Hence the practice of continuing one tablet of atabrine daily for three weeks following a therapeutic course of treatment.

The large scale experiments on human volunteers in Australia, which resulted in the demonstration of the ability of atabrine to eradicate falciparum infections while vivax infections were merely suppressed, also confirmed previous observations. The patient's blood, when transfused into other individuals, is not infective between 30 minutes after the bite and sixth to eighth day. This is excellent evidence to suggest the existence in man of an exo-erythrocytic stage similar to that observed in various species of bird malaria.

When the supplies of quinine were threatened, thousands of compounds were tested for anti-malaria activity against bird malaras. Those which showed promise were then tried out against human species



of malaria. The drugs mentioned so far all appeared to attack the younger asexual forms of the parasite or the gametocytes. One which seemed to affect the exo-erythrocytic stages of bird malaria more than others was paludrine. This drug seemed to attack the dividing forms of the human parasites as well.<sup>6, 7, 8</sup> Preliminary reports first appeared in 1945.<sup>9</sup> Given for 10 days it will eradicate falciparum infections while relatively small single doses will control the attacks of either vivax or falciparum.

If given during the incubation period, when parasites are not yet present in the peripheral blood, paludrine evidently attacks the dividing forms of the pre-erythrocytic stages. Single doses, given during this period will completely suppress all falciparum infections and a high percentage of vivax as well.<sup>6</sup> It is thus a true prophylactic as well as a therapeutic drug. Much work remains to be done in investigating this most promising compound.

The problem of the relapsing type of vivax remains. This has received so much publicity that its importance has been somewhat exaggerated. The Navy's figures for 10,000 cases from the Pacific area reveal that: 61 per cent had one relapse; 27 per cent had two relapses; 9 per cent had three relapses; 2 per cent had four or more.

These persistent relapsers are a problem to themselves as well as to their physician. A very careful history usually reveals sojourn in New Guinea, Guadalcanal, Leyte or Luzon, frequently with long periods of adequate atabrine suppression. One or more attacks may have taken place overseas or may have been delayed for months after return to the U. S., even a year or more after atabrine has been discontinued.

In many instances, self-treatment with inadequate amounts of atabrine or quinine for one to three days has resulted in an individual attack being continued over several weeks. Each febrile incident was counted as an "attack" which might result in a formidable total. One patient complained he had suffered 45 attacks which careful analysis reduced to 14. Such a history may

frequently reveal a surprisingly regular periodicity of relapse which may be very useful in anticipating further attacks.

It is important that these cases receive an adequate amount of therapy for each episode, as approximately 50 per cent are terminated. Frequent blood examinations for the slightest symptoms, especially during the expected period, will allow treatment to be initiated before symptoms become severe. Where the attacks are frequent and at short intervals it may be well to try a combination of quinine and plasmochin for 10 to 14 days. If available, a further new drug—pentaquine—has been shown to be most effective in the cure of relapsing vivax infections. It must be administered every four to six hours day and night for 14 days together with 0.3 gm. of quinine.<sup>10</sup> Since this tedious treatment will only be practical in a limited number of cases, preferably hospitalized patients, it seems these individuals would best be served by early prompt anticipatory blood examinations and treatment with chloroquine or a continuous and indefinite suppression with chloroquine or paludrine by unit doses once weekly.

Herewith is appended in tabular form a summary of the important information relating to the six drugs already mentioned.

#### QUININE AND THE CINCHONA ALKALOIDS

There are several salts of quinine: sulphate, bisulphate, dihydrochloride, bromate, tannate, and so on. Totaquine contains 70 per cent of all the crystalline alkaloids of the cinchona bark, quinine, quinidine, cinchonine and cinchonidine. Totaquine U.S.P. is used orally in the same dosage as quinine.

Quinine is readily absorbed and a peak plasma concentration is reached within four hours but it is equally rapidly excreted. The efficient blood level of 3 to 5 mgm. rising to 10 mgm. per liter should be maintained for several days.<sup>12</sup> Quinine sulphate or dihydrochloride 1.0 gm. (15 gr.) in capsule or tablet form is given every six hours for three doses and then 0.6 gm. (10 gr.) three times daily for a total of seven and sometimes ten days. Quinine should not be used

TREATMENT OF MALARIA INFECTIONS

"Any person, irrespective of the presenting symptoms or absence of same, who has lived in or merely passed through an endemic area, should be considered to have malaria until proven to the contrary."

The immediate attack=primary or relapse.

SPECIES	DRUG	INDIVIDUAL	The underlying infection =	falciparum malaria can be eradicated by atabrine, chloroquine and paludrine over maximum period indicated below.
				vivax (and quartan) malaria may relapse; 50+ % may be cured by adequate treatment of first attack.

DRUG	QUININE	PLASMOCHIN	PENTAQUINE SN 13,276	ATABRINE	CHLOROQUINE SN 7,618	PALUDRINE M-4888 SN 12,837
Dose	0.6-1.0 gm.	0.010 gm with quin. after At.	0.010 gm. +quin. 0.3 q. 4-6 hrs.	0.100 gm.	0.500 gm.	0.100 gm.
Frequency	t. i. d.	t. i. d.		t. i. d. after first 24-48 hrs.	u. i. d. after first day	b. i. d.
Duration (days)	7-10	5-14	14	7	3-4	1-14
Bl. level	3-10 mgm. L.	?	?	40-100 y per L.	100-160 y per L.	25-150 y per L.
Toxicity	nil side effects controls	yes	1 <sub>3</sub> —1 <sub>2</sub> of plasmochin cures	nil; yellow color cures	nil; rare side effects cures	nil cures
Falciparum infection		cures	cures			
Vivax relapses	early	decreased	80+ % cures	delayed	delayed	less delayed
Suppressive dosage	0.6 gm. daily	—	—	0.1 gm. daily	0.25 gm. weekly	0.1 gm. weekly

in areas where blackwater fever is known to occur. Ampules of various salts of quinine are available, usually in amounts of 0.5 and 1.0 gm. in 5 to 20 c.c. of solution, for parenteral use.

Plasmochin (plasmoquine, pamaquine U. S. P., pamaquin B. P., aminoquin, plasmochin naphthoate), is n-diethylaminoisoamyl-8-amino-6-methoxyl quinoline naphthoate. This, the first of the synthetic anti-malarial drugs; stopped schizogony and cured the clinical attacks of vivax and quartan malaria but gave indifferent results with falciparum. It did, however, sterilize the gametocytes, especially the more resistant falciparum gametocytes. In high doses it even neutralized sporozoites but these dosages were too toxic. Used in doses of 0.01 gm. three times daily for five days during the last five days of quinine therapy or beginning three days after atabrine therapy has been stopped, gametocytes are eliminated and in some areas seems to have had some effect in reducing the number of

relapses. More recently, quinine and plasmochin have been used together for 14 days in the treatment of persistent relapsing vivax infections. Atabrine tends to augment the toxicity of plasmochin and the two should never be given simultaneously. At the first sign of epigastric pain, blueness of the lips and shortness of breath, plasmochin should be discontinued. Excessive dosage produces hemoglobinuria.

Pentaquine (SN 13,276) is 6-methoxy-8-(5-isopropyl amino amylamino) quinoline monophosphate, a yellowish crystalline substance moderately soluble in water. Rapidly absorbed and rapidly excreted, the administration is at frequent intervals day and night and its effect is enhanced by the simultaneous ingestion of quinine. It is said to be one-third to one-half as toxic as plasmochin and is thus unsuitable for unsupervised treatment or for suppression but gives a high proportion of cures in relapsing vivax malaria. Tablets of 0.01 to 0.025 gm. are given together with 0.3 gm.



quinine every four hours for 14 days.

Atabrine (atabrin, atebirin, chinacrin dihydrochloride, quinacrine U. S. P., mepacrine B. P., metoquina, etc.) is 3-chloro-7-methoxy-9-(1-methyl-4-diethylamino) acridine dihydrochloride, a bitter, bright yellow dye. Since the tissues must first be saturated by the drug the plasma level rises slowly until an effective level of approximately 30 micromilligrams per liter is reached. Two 0.1 gm. tablets are given every four to six hours for the first 24 to 36 hours, then one tablet three times daily for a total of seven days when approximately 3.0 gm. have been ingested. In falciparum infections, one tablet is continued for a further 21 days. Atabrine dihydrochloride 0.2 gm. in ampules is available for parenteral administration. This amount, dissolved in 5 to 7 c.c. of sterile distilled water, is injected intramuscularly every six to eight hours until the severe symptoms have abated or oral administration is tolerated. Two-tenths gram of atabrine in 10 c.c. of distilled water or added to infusions of larger volume up to 500 c.c. are given very slowly intravenously. The unfavorable reactions to intravenous atabrine which have been reported were usually with other preparations of the drug or with doses much higher than stated here.

Where nausea and vomiting are present or threaten, when the patient is acutely ill, parenteral atabrine or quinine should be used promptly. In dangerous falciparum infections, especially where there are signs of shock or cerebral involvement, one should not hesitate to give the drugs intravenously.

Chloroquine (resochin, sontochin, aralen) is 7-chloro-4-(4-diethylamino-1-methylbutylamino) quinoline diphosphate, a white crystalline powder. It has the same therapeutic properties as atabrine,<sup>15</sup> but acts more quickly with fewer doses and has no objectionable color. Parasites disappear from the blood very quickly. The blood plasma level of 50-200 micromilligrams per liter is obtained during therapy.<sup>14</sup> Four 0.25 gm. tablets given on diagnosis, two tablets six hours later and then two sim-

ilar tablets each morning for two or at most three successive days, constitute the entire treatment for an individual attack.

Paludrine (SN 12,837, M-4888) is N1-chlorophenyl-N5-isopropyl biguanide acetate, a somewhat soluble white powder.<sup>13</sup> In contrast to the preceding drugs, paludrine appears to have some direct effect on the non-erythrocytic forms of malaria parasite as well as the asexual symptom-producing stages. It has been shown to be a complete causal prophylactic in falciparum malaria.<sup>6</sup> The blood level varies with the dosage used from 25-1200 micromilligrams, the concentration in whole blood being about four times that of plasma. Paludrine is rapidly absorbed with maximum levels obtained in four hours, falling off in 12 hours with increasing levels if taken twice daily. Tablets of 0.100 gm. are available and while single doses of 0.050 gm. to 0.300 gm. have controlled individual attacks, one tablet thrice daily for 10 days or twice daily for 14 days is advised for the eradication of falciparum malaria. Chronic relapsing vivax malaria is not cured but one tablet every five to seven days is sufficient to abolish symptoms and may contribute to an ultimate cure.

#### SYMPTOMATIC TREATMENT

In addition to the specific treatment, supportive treatment and good nursing care will do much to lessen the severe discomfort of the malaria attack. The individual vivax paroxysm may be much more severe than one due to falciparum. Bed rest, abundant fluids with glucose and fruit juices may be given while additional sodium chloride may be required. For the first two days, 1.0 gm. of sodium bicarbonate may well accompany each dose of quinine or atabrine. Purgation only increases the patient's discomfort so an enema should be given if required. An electric pad if available or hot water bottles are more effective than blankets during the chill period. Frequent changes of bed and body clothing are necessary and appreciated. The diet should be as generous as the patient can take. Post-treatment with ferrous sulphate 0.6 gm. thrice daily may well be given if

any degree of anemia has resulted.

#### PROPHYLAXIS AND SUPPRESSIVE MEDICATION

Many years ago, the daily taking of 5 grains of quinine was found to reduce appreciably the amount of malaria among non-immune people in some of the most unhealthy parts of India and Africa. Later it was seen this amount was inadequate and the daily dose was increased to 10 grains. Neither quinine, atabrine nor chloroquine are prophylactics in that they prevent the infection developing. They merely, when taken regularly, keep the infection below clinical levels, hence the term suppression. When this form of medication is discontinued clinical activity, particularly of vivax infections, may occur. Delayed primary attacks have appeared from 30 days to 18 months after discontinuance of suppressive quinine and atabrine. Thus, suppression is a matter of expediency rather than a sound method of malaria control. Atabrine and chloroquine are more efficient than quinine as suppressives in that falciparum infections may be acquired and eradicated without ever developing to clinical levels.<sup>4</sup>

Paludrine, in addition to acting as a suppressive if taken from the second to fifth day of a known sporozoite inoculation, can stop all falciparum and some vivax infections in the non-erythrocytic stage. It is, thus, a true causal prophylactic.

Plasmochin and pentaquine are too toxic for continued use as suppressives.

The efficient dose of each of the other drugs and the frequency of their administration is shown in the table. Persons showing an idiosyncrasy to any two of the above drugs should not be permitted to go to any area of high malaria endemicity.

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#### DISCUSSION

*Question:* Dr. Walker, is this pentaquine quite toxic?

*Dr. Walker:* It is apparently a third to a half as toxic as plasmochin.

*Question:* How toxic have you found plasmochin?

*Dr. Walker:* In our experience we have not very often found toxic effects but when they occur they have been quite severe. I feel if people are going to have toxic reactions with plasmochin they may have reactions to pentaquine as well.

*Question:* How long do you keep up chloroquine?

*Dr. Walker:* We treat the individual attack as suggested here. The first day we give one gram, four tablets, on diagnosis, and six hours later two tablets and then on three successive mornings—two tablets. The mimeograph form is not quite complete on that. That is the complete treatment until the next attack.

*Question:* You do not keep up suppressive treatment?

*Dr. Walker:* No, unless relapse is too frequent. I have a young man going to school at Tulane. He worries about his examinations and does not want an attack to cause him to miss any of them. He does not like to take a chance so we give him paludrine every five days; one tablet, or he could take chloroquine. The best way is to treat the attack and then wait for the next attack.

*Question:* Routinely, you do not advise once a week?

*Dr. Walker:* No. If a patient is having attacks under two months and he has a good many and is



tired of them, all well and good, give chloroquine suppressively for three to six months. As some patients are likely to drop out after each treatment, how are you going to find out if the infection is worked out and finished when you keep up suppression on them all the time. We are seeing this year one-third or one-quarter as many patients as we saw last year. These Pacific cases are running out at a tremendous rate. My own opinion is that after three years they will be extremely rare. If the attacks are frequent and troublesome and you cannot anticipate because they do not show any regular periodicity, examine the blood at frequent intervals. The patient should not have to go to bed with the attack. Several have not been in bed for some time. I may say about paludrine that it seems to be a tremendously effective drug. It is obviously a drug for suppression and very small doses will control an individual attack. We are using 300 mg. temporarily but actually 100 or 150 mg. have been given with apparently no increase in relapse. The sheet there indicates the suppressive treatment—one paludrine tablet every seven days. There is no rule of treatment. The individual case should be treated according to its behavior. Paludrine should be available in the New York market very shortly. It is available in England at the present time. Chloroquine has been on the open market since October. The great advantage of chloroquine is the total treatment time is four days and people who are over their symptoms universally are neglectful of further medication so that my own opinion at the moment is that paludrine will be the drug of suppression and chloroquine the drug of treatment.

*Question:* Have you had any failures with atabrine in cases that responded to other drugs like chloroquine?

*Dr. Walker:* I have not had failures with atabrine where doses have been adequate. There are failures with insufficient doses; the attacks merely interrupted, not checked.

*Question:* I had one patient in the hospital who did not respond and gave chloroquine and he responded.

*Dr. Walker:* It is dramatic how quickly chloroquine clears the blood of parasites. Paludrine does not behave that way. It seems to attack parasites in segmenting stage and they are then found in this stage for two, four or six days.

*Question:* What about the effect of the drug on quartan type? We are not free of this in our community but hope we might be.

*Dr. Walker:* As you know we do not have sporozoite induced quartan at the present time but the needle induced quartan behaves clinically the same and reacts to the drugs identically as does vivax. Quartan is perhaps a little slower to be cleared from the blood with chloroquine but it is cured in the same way as vivax. It is not necessary to give more than a single dose of paludrine for treatment of needle induced vivax or quartan infections.

## ENTERIC INFECTION OR INFESTATION SINE DYSENTERY\*

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AND

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Since biblical times dysentery has been recognized as one of the common diseases. Until recently diarrhea has been considered a symptom essential to the diagnosis. The identification of *E. histolytica* by Loesch in 1875 and of *B. dysenteriae* by Shiga and Kruse in 1897 did not change this thought although these discoveries helped enormously to clarify the subject of the diarrheal diseases. Acute dysentery with its typical clinical picture has never posed a diagnostic problem, nor has chronic dysentery, when characterized by irritative bowel manifestations of lesser severity but greater duration than the acute disease. In this presentation there will be considered a less generally appreciated type of chronic dysentery with symptoms different from those of the typical diarrheal group.

Although the word "dysentery" has been loosely applied to diarrheas generally, it has been limited by medical definition to disease caused either by *E. histolytica* or by a member of the Shigella group. In 1945 Silverman and Leslie<sup>1</sup> presented the first of a series of cases of chronic Salmonella infection clinically indistinguishable from the chronic cases of "dysentery tardive" under discussion. These cases of chronic Salmonella infection have been shown<sup>2</sup> to constitute a formidable group, and so are being included here.

During the past three years 123 unselected private cases of proved enteric infection or infestation were studied. For several reasons these do not represent a fair sampling of the general run of the dysenteries. First, it must be remembered that acute bacillary dysentery is a self-limited disease except for the 15 to 20 per cent of cases which become chronic, and is normally han-

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dled by the family physician, not by the gastroenterologic consultant. Second, previously proved cases of enteric infection or infestation seen by the gastroenterologist are usually those which have not responded favorably to methods of therapy available to the general practitioner, and have become chronic, or those which have been low grade and chronic from the outset. In addition, the gastroenterologist sees patients with abdominal complaints of more or less obscure nature, a fair proportion of whom will prove to have specific enteric disease.

The group of cases which comprises the substance of this paper is an important one, not only in the South but over the entire country. It is safe to assume that where there is acute dysentery, chronic dysentery is likely to occur. This is well appreciated in the South, but is perhaps less so in other parts of the country, where such relatively minor abdominal complaints as lead Southern physicians to suspect the presence of dysentery are not generally associated with the possibility of enteric infection or infestation. It is well known that acute dysentery occurs commonly in the more temperate as well as in the subtropical areas of the United States. Local outbreaks have been reported in Washington, Illinois, Michigan, New York, Canada, and other Northern as well as Southern localities.<sup>3-7</sup> Since the specific organisms have been shown to thrive in Northern as well as Southern environment, chronic dysentery is probably prevalent over our entire country. An increasingly important cause of the dissemination of this disease in the United States is the apparent relaxation of quarantine regulations, and, with the expansion of travel facilities, both air and sea, the swelling influx of our good neighbors to the south.

Chronic dysentery and the carrier state are endemic in Latin America and, as foreseen by Silverman<sup>8</sup> in 1926, have become so in the United States. Figures vary, but it has been conservatively estimated<sup>9</sup> that the *E. histolytica* is harbored by 5 to 10 per cent of the population of the United States and by a much higher percentage of the

peoples of Latin America. It is perfectly obvious, however, that clinical amebiasis occurs in far smaller percentages. On the other hand, it must be apparent that minor complaints of indigestion, deemed hardly worthy of a doctor's attention unless recurrent and disturbing, may result from potentially serious enteric disease. What is becoming generally known about chronic amebic disease of the colon must be equally true of chronic bacterial disease, since in the present series of 123 unselected cases there was no diagnostic differentiation on the basis of symptomatology among the cases of amebic, Shigella, or Salmonella disease. Physical and proctoscopic examination only occasionally aided this differentiation, the diagnosis being established by laboratory examination and confirmed by response to therapy.

Here we are not dealing with obvious disease with the easily visible diffuse mucosal inflammation of bacterial infection or with the discrete undermined ulcers of amebiasis. These chronic cases, especially the ones without diarrhea, may have a pathology no more extensive than a few scattered lesions in the cecum and ascending colon, always, however, with the Damocleian threat of rapid dissemination. It is easy to see how this type of pathology may give rise to less typical symptoms or be referred to a remote location, in or out of the gastrointestinal tract.

Table 1 illustrates the type and frequency of symptoms seen in these cases. No statistically significant differences can be drawn to associate particular symptoms with specific organisms. What is of principal clinical significance is the absence of any history of diarrhea in 43 cases and the existence of actual constipation in 24 cases. Diarrhea as a chief complaint was noted in only 13 cases, although 20 gave a history of severe acute diarrhea in the past. Thirty-nine patients reported occasional or recurrent diarrhea. Epigastric pain occurred in 20 patients, and in some was associated with other so-called gastric symptoms. Melena occurred in 16 of the cases of amebiasis but in only eight of the cases of bacterial



TABLE 1

	E. Histolyt.	Flexner	Shiga	Duval-Sonne	Para A.	Para B.	Total
Diarrhea as							
chief complaint	3	4	0	2	1	3	13
Past history of							
acute diarrhea	9	5	0	1	1	4	20
History of recurrent							
or occasional diarrhea	12	14	5	0	2	6	39
No history of diarrhea	20	10	4	5	1	4	44
Constipation	9	6	4	5	0	0	24
Abdominal pain;							
diarrhea	10	6	2	2	1	6	27
Abdominal pain;							
no diarrhea	17	11	5	4	1	6	44
Epigastric pain	13	6	4	3	0	3	29
Nausea	5	2	3	1	3	3	17
Pyrosis	9	1	0	1	1	1	13
Melena	16	4	1	1	0	2	24
Fever	1	4	0	1	1	3	10
Weight loss	4	5	4	1	0	6	20
Lassitude	3	3	2	0	1	2	11
Miscellaneous (headache,							
backache, flatulence,							
arthritis, neuralgia,							
dysmenorrhea)	17	7	2	1	1	4	32
Number of cases	51	33	9	8	5	17	123

disease. The less specific symptoms appeared about uniformly among all the groups, and it was not possible to demonstrate that there was any greater incidence of complaints in any single group.

Particular attention is directed to the cases of chronic *Salmonella* infection. From the table it is seen that there is nothing characteristic to distinguish these cases from the true dysenteries. Within the limits of the number of cases presented, the minor percentage differences cannot be considered significant, whereas the over-all similarities are apparent.

In considering therapy and the results thereof, sharp distinction must be made between protozoon and bacterial disease. The cases of amebiasis were given specific treatment, usually emetine plus diodoquin or carbarsone. Following three or four weeks of therapy, with few exceptions, cure was obtained, and confirmed by repeated subsequent examinations. The sulfonamides having been found to be of little or no value in the management of chronic cases of intestinal infection, we are still faced by the lack of specific therapeutic agents. Therefore, these cases received, in addition to

aggressive supportive therapy, extended courses of autogenous vaccine desensitization. The results of treatment over periods of several months to two years have been generally satisfactory, although the definite end-point of cure as seen in amebiasis has not been observed. Anti-amebic therapy caused rapid regression and disappearance of the colonic lesions which were within view of the sigmoidoscope. On the other hand, disappearance of signs of bacterial disease, such as ulceration, mucosal hyperemia, vasodilatation, submucosal lymphatic hypertrophy, and the presence of excess mucus was slow. The sigmoidoscopic signs and progress were identical in both *Shigella* and *Salmonella* disease. Some of these cases, although subjectively improved after long continued treatment, continued to harbor the organism and showed little or no improvement in the bowel. Some observers, particularly Felsen,<sup>10</sup> would incline to classify these as cases of ulcerative colitis, caused by specific organisms, but evidence for this contention is not convincing.

#### DISCUSSION

The observations made do not apply to acute dysentery, which constitutes the large

majority of clinically recognized cases of infection or infestation of the bowel, but to the less generally appreciated but equally important cases of chronic dysentery. The importance of the chronic type of the disease stems not only from the diagnostic standpoint but from the public health consideration as well, since epidemics can and almost certainly have originated from such cases which have escaped detection.

The absence of irritative bowel symptoms or a history thereof does not negate the possibility of specific enteric disease. A history of sporadic loose bowels, perhaps only in the distant past, is helpful to direct attention to the bowel as a possible site of present disease, but even this history may not be educible. In this connection it is well to remember that it is frequently difficult to obtain bacteriologic proof of infection. Repeated culture of bowel scrapings obtained proctosigmoidoscopically may be necessary before a positive culture is reported. In the face of often frank pathology, the reason for this is not clear.

In considering the bowel pathology visible on endoscopic examination, it may suffice to state that in chronic bacterial dysentery there is variation from a practically normal appearance to one of severe inflammation with diffuse redness, vascular engorgement, mucosal edema and ulceration, and areas of submucosal lymphatic hypertrophy. Cases of amebiasis, similarly, may present no apparent abnormality or may show anything from minor to extensive ulcerative involvement. Roentgenographic examination of the colon may show no abnormality or may show local or diffuse irritability, but not the changes seen in chronic ulcerative colitis, unless this disease co-exists, as it did in two of the cases presented. X-ray study of the small intestine frequently shows the pattern described by Golden<sup>11</sup> as occurring in secondary deficiency states, and by Silverman and Leslie<sup>1</sup> as occurring in chronic *Salmonella* infection.

The inclusion of cases of *Salmonella* infection in a discussion of dysentery may

seem open to dispute. But these cases presented no feature which could serve to distinguish them from the cases of chronic *B. dysenteriae* infection, clinically, sigmoidoscopically, or radiologically; only the bacteriologic differentiation obtained. They bore even less similarity to paratyphoid fever than the cases of chronic dysentery did to acute dysentery.

It is therefore submitted that the definition of dysentery should be broadened to include such cases of chronic *Salmonella* infection as satisfying the stated clinical, proctoscopic and radiologic criteria.

#### SUMMARY

1. Clinical, bacteriologic, radiologic, pathologic, and epidemiologic considerations in 123 unselected private cases of chronic enteric disease caused by *E. histolytica*, *B. dysenteriae*, and *B. paratyphosus* are presented, the frequent insignificance of diarrhea in the history being emphasized.

2. Since chronic *Shigella* and *Salmonella* enteric infection can only be differentiated bacteriologically, a brief is made for the incorporation of the latter into the dysenteries, and broadening the definition of dysentery to include the *Salmonella* as an etiologic agent is suggested.

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## EXTRA-INTESTINAL AMEBIASIS\*

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NEW ORLEANS

Amebiasis and its complications are problems of considerable incidence and importance which may perhaps become increasingly so with the return of so many individuals from areas more endemic than our own. Several excellent papers on various aspects of the subject have appeared during the past few years, but repetition and attention are perhaps justified in an attempt to provoke and maintain a high index of suspicion in a condition in which diagnosis is all the more important since definite specific therapy is available.

*Endameba histolytica* is estimated to exist in the intestinal tract of from 5 to 20 per cent of the general population<sup>1, 2</sup> and is capable of invading from this primary focus practically all of the organs and tissues of the body. The liver, lungs and pleura are relatively common sites of secondary amebic infection; involvement of the brain<sup>4</sup> and skin<sup>9</sup> occurs much more infrequently; and, while cases of amebic involvement of the spleen, genitourinary system, gall-bladder, bone and pericardium have been reported,<sup>1</sup> they are sufficiently rare to relegate them to the field of medical curiosities rather than practical clinical entities.

Amebic hepatitis and amebic abscess of the liver are by far the most common and certainly the most important complications of amebiasis. Amebic infection of the liver occurs ten times more frequently in the male than in the female and is most common in the 30-50 year age group.<sup>6</sup> It is estimated to complicate about 5 per cent of intestinal amebiasis<sup>6</sup> and includes about 50 per cent of the surgical complications of amebic infection.<sup>5</sup> In a review by Ochsner and DeBakey<sup>6</sup> of 287 cases of liver abscess admitted over a 14 year period to Charity Hospital and Touro Infirmary in New Or-

leans, it was found that 181 (63 per cent) were amebic and 106 (37 per cent) were non-amebic.

The amebae may gain access to the liver by direct invasion, by lymphatic spread or by way of the portal circulation. There seems little doubt that invasion by way of the portal circulation is by far the most common, if not the only, route of entry. Once the organism has reached the liver, local vessel thrombosis occurs followed by infarction with dissolution of tissue by the cytolytic ferment of the ameba, carrying the process to abscess formation. Amebic abscesses are more frequently solitary (65 per cent and are more commonly found in the right lobe (85 per cent), usually near the dome of the liver.<sup>7</sup>

Only about half of the cases of amebic abscess of the liver give an antecedent history of diarrhea. The dysenteric symptoms have usually occurred within two or three months previous to the liver involvement, although cases have been reported in which amebic dysentery antedated the liver complication by 20 to 30 years. The onset may be sudden or gradual with fever, chills, sweats, weakness, loss of weight and pain in the right upper quadrant or right lower chest region. The pain may be deep and constant or it may assume the character of pleuritic pain with aggravation upon inspiration and referral to the right shoulder region as a result of involvement of the diaphragmatic pleura. Tenderness and increased resistance are usually present in the right upper quadrant. Some degree of hepatomegaly is almost invariably present. There may be diminution of breath sounds and resonance along with a few fine rales over the right posterior lung base as a result of compression atelectasis from elevation and reduced mobility of the right hemi-diaphragm.

Laboratory procedures may be very valuable in confirmation of the diagnosis. A moderate leukocytosis is usually present; however, in the presence of secondary infection the leukocyte count may be quite high. Demonstration of amebae in the stool depends to a large degree on the care and frequency with which stool examination is

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done. In several large series of cases of amebic hepatic abscess, stools have been found positive for ameba histolytica in 11 to 36 per cent of cases.<sup>6</sup> Proctoscopic examination may be helpful in visualization of ulceration in the lower bowel and in obtaining material for microscopic examination. The complement fixation test is of apparent value, but the difficulty at present in preparation of the antigen precludes its general use.<sup>3</sup> X-ray examination is unquestionably the most valuable laboratory procedure in that 85 to 90 per cent of cases may be expected to show positive roentgenographic signs.<sup>6</sup> These consist in the main of elevation and immobility with or without local bulging or "steeppling" of the right hemi-diaphragm. The use of thorium dioxide and lipiodol have been advocated by some observers as an adjunct in roentgen diagnosis of hepatic abscess.<sup>10</sup> However, in light of our incomplete knowledge of the effect of these substances on the liver, their use is not generally recommended.

The complications of amebic abscess of the liver are concerned with secondary infection and rupture into adjacent tissues. The more common sites of rupture are into the lung, pleural space and peritoneal cavity. Occasionally rupture may occur into the pericardial cavity or some adjacent organ such as the spleen, kidney or colon.

The treatment of amebic abscess is, in the main, conservative consisting of the administration of emetine hydrochloride (gr. 1 daily subcutaneously for 7 to 10 days) with or without aspiration of the abscess. In general, it may be said that most cases will require one or two aspirations. Some cases, however, subside with the use of emetine alone. At times, the decision to aspirate is not easily made; one must be guided by the degree of the response to emetine and the presence or progression of the x-ray signs of bulging or "steeppling" of the diaphragm. The pus obtained by aspiration is usually of the typical reddish-brown "anchovy sauce" type, contains demonstrable amebae rather infrequently, and is sterile unless secondary infection has occurred. There seems to be no virtue in

the instillation of emetine hydrochloride into the abscess cavity; perhaps, the instillation of penicillin into the abscess cavity after aspiration may retard or prevent the occurrence of secondary infection. Open drainage is indicated only after secondary infection has occurred.

In addition to the general factors of virulence of the organisms and host resistance, prognosis depends on the multiplicity of the lesions, presence or absence of secondary infection and other complications, and the type of therapy employed. Review of analysis of a large series by Ochsner and DeBakey reveals the following approximate overall mortality figures: 10 per cent in cases with solitary abscesses; 60 to 100 per cent in those with multiple abscesses; about 40 per cent in complicated cases and about 75 per cent in those cases with secondary infection. In general, the mortality with open drainage is about seven to eight times that with the more conservative aspiration procedure. In a collected series of about 5,000 cases, the mortality from open drainage was 45 per cent, while only 6.7 per cent in those treated with emetine and aspiration.<sup>7</sup> The decline in overall mortality of amebic liver abscess is strikingly proportional to the gradual acceptance of aspiration and emetine as the therapy of choice.

#### PLEUROPULMONARY AMEBIASIS

Although cases of supposed primary amebic pneumonitis have been recorded, it seems doubtful that primary infection of the lung occurs in the absence of previous bowel infection. Probably 75 per cent or more of amebic pleuropulmonary involvement occurs as a complication of rupture of an hepatic abscess through the diaphragm, and it is likely that the remainder result from hematogenous spread from the intestinal tract. About 15 per cent of amebic liver abscesses are complicated by pleuropulmonary lesions which may take the form of a bronchohepatic fistula, a lung abscess, or an empyema, or any combination thereof.

The clinical manifestations of pleuropulmonary involvement vary according to the mode and extent of the infection. In amebic



lung abscess of hematogenous origin the clinical picture is little different from that seen in pyogenic lung abscess. In cases which complicate liver abscess, pleuritic pain in the right lower chest accompanied by dyspnea and an unproductive cough, together with an increase in the gravity of the patient's general symptoms, usually herald the extension of the process into the chest. Expectoration of anchovy sauce sputum containing *Endameba histolytica* is practically pathognomonic of bronchohepatic fistula. The physical findings over the right lower chest may be those of fluid, consolidation or cavitation depending on the dominant process present. However, the usual findings are inspiratory lag, dullness, suppression of breath sounds and fine rales. The x-ray findings are usually those of pleural reaction, fluid and consolidation in the lower half of the lung field. However, in some cases, the roentgenographic findings are quite characteristic, showing a triangular density extending from a high right hemi-diaphragm toward the hilus of the lung.

Treatment is generally conservative. In cases with bronchohepatic fistulae the administration of emetine hydrochloride and postural drainage is usually all that is necessary. Aspiration should be done if pleural effusion is present. Open drainage is reserved for those cases in which definite secondary infection of the pleural space has occurred.

Prognosis depends largely on the type of involvement and the therapy employed. Bronchohepatic fistula and lung abscess communicating with a bronchus allowing for good drainage carry the best prognosis, mortality being 5 to 10 per cent, whereas in those cases with empyema mortality greatly increases to about 75 per cent.

#### BRAIN ABSCESS

Amebic brain abscess occurs relatively rarely and almost never in the absence of amebic infection of the liver and/or lungs. The clinical picture is much the same as that presented in pyogenic abscess except that the course toward an invariably fatal

termination in spite of therapy is inexorably more rapid.

#### AMEBIASIS CUTIS

Ulceration and abscess of the skin is a rare complication of amebiasis and usually occurs as a secondary manifestation of rupture or drainage of an hepatic or pericolic abscess through the skin. Occasional cases have been reported as a result of perianal extension of amebic rectitis. Clinically, there is swelling and induration followed by necrosis resulting in an ulcerated area having an irregular contour with gangrenous overhanging edges. The condition is similar in appearance to the post-operative synergistic gangrene described by Meloney due to microaerophilic nonhemolytic streptococci. Amebae may be demonstrated in necrotic tissue removed from the edges of the ulceration. Treatment consists in the administration of emetine hydrochloride and wide excision of the ulcerated area with the high-frequency knife. Wyatt and Buchholz<sup>9</sup> reported a mortality of 42.3 per cent in a review of 26 cases.

#### SUMMARY

Extra-intestinal amebiasis is discussed relative to its incidence and importance. Diagnosis and management of hepatic and pleuropulmonary involvement are dealt with in some detail. Conservative therapy with emetine hydrochloride and aspiration is emphasized.

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## AN EVALUATION OF ANTI-AMEBIC DRUGS

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### INTRODUCTION

By definition the clinical term "amebiasis" includes all conditions caused by the invasion of the tissues of man by the pathogenic ameba known as *Endamoeba histolytica*. The invasion of the various tissues of the body occurs primarily through the mucous membrane of the large intestine and less often through that of the lower portion of the ileum. The term "amebic dysentery," formerly used to indicate all infections with *Endamoeba histolytica*, with the exception of amebic abscesses of various organs, is now properly restricted to infections in which the prominent symptom is a bloody diarrhea induced by this parasite.<sup>1</sup>

The problem of treating amebic infection is arousing great interest among medical groups throughout the countries of the world. While military medical men have been conducting first-hand, battle-front re-research in the treatment and control of amebiasis throughout the world, civilian research has been continuing through the war years in America. From the islands of the Pacific, from the Orient, from the Mediterranean area and from countries all over the world have come reports on various drugs used in the treatment of this scourge of amebic infection which has plagued armies and peoples throughout history. Many strides have been made as a result of wartime research in amebiasis.

The end of the war, however, has not lessened the problems of amebiasis control. On the contrary, it has brought them closer home. As millions of our military men and women have already returned to America from regions where amebiasis is endemic or even epidemic, there is an obvious likelihood of a greatly increased incidence of amebic infections in this country. An evaluation of the research in amebiasis and the drugs used in the treatment of this condition is necessarily in order at this time. In this paper the writer will attempt to pro-

vide a concise summary of the medical developments which have taken place in the treatment and control of amebiasis during the past five years or so.

### HISTORY

The causative organism of amebiasis and amebic dysentery was first discovered in 1875 by Lösch while examining a stool of a patient with dysentery in St. Petersburg, Russia. At that time he gave to the pathogenic organisms the name of "*Amoeba coli*," but this has since been changed to *Endamoeba histolytica*. It is still questionable whether other observers had seen this ameba prior to Lösch. However, it is generally believed that the credit for the discovery of the pathogenic species belongs to him.

Koch, in 1883, observed five cases of dysentery in Egypt, two of which were complicated with abscess of the liver, and in the ulcers occurring in the large intestine he found numerous amebae and in sections these were also found deep in the tissues at the base of the ulcerations, as well as in the capillaries of the liver, close to the abscess walls.

In 1886, Kartulis published a paper describing his results in the study of 150 cases of dysentery in Egypt in all of which he demonstrated amebae identical with those described by Lösch. Also Kartulis was successful in producing dysentery in cats by rectal injection of feces containing amebae.

Sir William Osler, in 1890, was the first one in the United States to demonstrate the amebae in a case of dysentery and liver abscess, and his observations were followed in the same year by those of Stengel. In 1891, J. H. Musser, Sr.,<sup>2</sup> at the University of Pennsylvania also demonstrated amebae in a case of dysentery complicated by abscess of the liver. This was followed in the same year by the work of Dock.

One of the classics on the subject of amebiasis was published in 1891 in the form of a monograph by Councilman and LaFleur who reported on 14 cases studied at the Johns Hopkins Hospital. They concluded that amebic dysentery is a clinical entity



and that it is characterized by definite pathologic lesions produced by the amebae.

In 1893 and 1894, Quincke and Roos published the first description of the cysts of *Endamoeba histolytica*. A more accurate description of the cysts of this parasite was published by Huber in 1903. Schaudinn in 1903 accepted the name for the genus previously proposed by Casagrandi in 1895, but named his pathogenic species, *Endamoeba histolytica*, and the name *Endamoeba coli* to the non-pathogenic species.

The first observer to produce an abscess of the liver in an experimental animal after the production of dysentery by the rectal injection of *Endamoeba histolytica* was Harris (1901). Later amebic abscess of the liver was produced in this manner by Craig (1905), Huber (1909), Wenyon (1912), Baetjer and Sellards (1914), and Dale and Dobell (1917).<sup>1</sup>

#### GEOGRAPHIC DISTRIBUTION

Amebiasis is worldwide in distribution. It can no longer be considered a tropical disease. Craig<sup>1</sup> states that the infection is widespread throughout the United States and conservatively estimates that from 5 to 10 per cent of the population of this country is infected with *Endamoeba histolytica* and that at least 50 per cent of individuals infected with this parasite have definite symptoms which are caused by its presence. Faust<sup>3</sup> believes that the incidence in this country may well be even higher than 5 to 10 per cent because the samplings of the population are perhaps too scattered and isolated to be completely representative of the degree of infection.

While amebiasis has a world-wide distribution the severe lesions and symptoms which are present in amebic dysentery occur much more frequently in the tropics and the warmer portions of the sub-tropics than in temperate and cold climates. In the United States cases of amebic dysentery have been reported from practically every state in the Union and there can be no doubt that many cases are wrongly diagnosed annually, because of the widespread belief that this type of dysentery occurs only in the tropics or sub-tropics. According to Craig,<sup>1</sup>

amebic dysentery is most frequently observed in the United States in Louisiana, Texas, Georgia, Florida, California, Mississippi and Alabama, but a considerable number of cases have been reported from Virginia, Maryland, the District of Columbia, and the Carolinas.

#### CLASSIFICATION OF AMEBIASIS

Just as in the consideration of the symptomatology of amebiasis it is essential to understand the method by which *Endamoeba histolytica* produces lesions in the intestine and the character of these lesions, it is equally as essential in the choice of specific therapy to have a working, clinical classification of the disease. Specific treatment and the use of certain specific drugs will naturally vary with the location of the lesions and the severity of the infection.

Many clinical classifications of the various types of amebiasis have been proposed by different authorities but the following seem to be the most useful. Dobell and Low<sup>4</sup> in 1922 outlined the following simple classification: (1) carrier; (2) general amebiasis; (3) amebic diarrhea; and (4) amebic dysentery.

The clinical classification by D'Antoni,<sup>5</sup> a modification of Craig's classification, appears to be the most useful to the writer. It is based upon symptomatology and it should be remembered that the various clinical classes mentioned tend to merge into one another and that an individual who may be placed in one class may, at any time, develop symptoms characteristic of one or more of the other classes.

#### CLINICAL CLASSIFICATION OF AMEBIASIS

##### 1. *Asymptomatic amebiasis*

The patient is not cognizant of symptoms and the lesions are not confined to specific areas.

##### 2. *Symptomatic amebiasis*

a. *Asyndromic* (formes frustes): There is a mild toxemia and vague gastrointestinal irritation with lesions usually not confined to specific areas.

b. *Syndromic*: There may be symptoms simulating chronic appendicitis, peptic ulcer, chronic cholecystitis with lesions usually confined to the cecal area.

c. *Dysentery* (acute or chronic): There

are symptoms of dysentery with the lesions throughout the colon, especially the rectal and sigmoid areas.

d. *Hepatitis and liver abscess*: The symptoms usually are fever, pain and tenderness in the liver area with liver lesions.

e. *Involvement of other organs (extra-intestinal)*: Abscess of lung, brain, kidney, amebiasis cutis, and so on.

#### LOCATION OF LESIONS

The location of the lesion in the intestine is important from both a prognostic and therapeutic point of view. It has been found that the most advanced and oldest lesions will usually be found in the ileo-cecal region, including the ileo-cecal sphincter, the distal-most segment of the ileum, the cecum, the appendix and the ascending colon; next the rectum and sigmoid colon, then the sigmoid and hepatic flexures—regions where stasis of the fecal mass occurs most commonly.

Clark<sup>6</sup> (1925) found the order of frequency of ulceration was the cecum, ascending colon, rectum, sigmoid, and appendix. Craig<sup>7</sup> (1934) in 78 cases found lesions in the ileo-cecal region, the descending colon, and the rectum in 57 cases; lesions along the whole length of the colon in 12 cases, but most severe below the ileo-cecal valve and in the rectum; while in nine cases the rectum and the sigmoid alone showed active lesions, with healed lesions in the ileo-cecal region.

Faust (1940) and D'Antoni<sup>8</sup> (1941) found that the preponderance of lesions occurs in the cecal area and next in the rectal area and that these two levels of involvement primarily condition the types of symptoms in intestinal amebiasis, namely cecal amebiasis and sigmoido-rectal amebiasis.

#### CLASSIFICATION OF AMEBACIDAL DRUGS

##### A. *The Emetine Group*

1. Ipecacuanha (ipecac)
2. Emetine hydrochloride
3. Emetine bismuth iodide

##### B. *The Oxyquinoline Derivatives*

1. Chiniofon
2. Vioform
3. Iodoquin
4. Diodoquin

##### C. *The Organic Pentavalent Arsenicals*

1. Carbarsone
2. Treparsol
3. Acetarson

##### D. *Miscellaneous Drugs*

1. Succinylsulfathiazole
2. Penicillin
3. Trilactic
4. Kurchi bark
5. Bismuth subnitrate
6. Shadocol (sodium tetraiodophenolphthalien)

#### THE INDIVIDUAL AMEBACIDAL DRUGS

*Ipecacuanha*: This particular drug is the dried root of *Psychotria ipecacuanha* which is native in Brazil but is cultivated in India, the Straits Settlements, and the Federated Malay States. The efficiency of the drug is dependent on its two chief alkaloids, emetine and cephaline. Of the two alkaloids emetine is by far the more potent as an amebicide, although cephaline does possess some amebicidal action. This drug was used for years in the treatment of amebiasis by the natives of Brazil, on the European continent, and in this country. While the drug possesses all the amebicidal properties of emetine, its use in the modern treatment of amebiasis is definitely limited due to the difficulty of administration and the excessive discomfort caused by it.

*Emetine*: Emetine was first described in 1817 by Pelletier, the discoverer of quinine in cinchona bark. Bardsley in 1829 was apparently the first person to use emetine in diarrheas and dysenteries. In 1912 Vedder demonstrated that emetine is a powerful amebicide to free-living amebae in cultures, and the same year Rogers reported good results from the drug in the treatment of amebic dysentery and hepatitis.

Emetine is an alkaloid of ipecacuanha and is used in the form of the hydrochloride salt because of its greater solubility. It is prepared in ampules containing one grain of emetine hydrochloride in 1 c.c. of solution. The dosage for adults consists of one grain subcutaneously, not to exceed 12 grains within a period of 40 days. The drug should never be given to children under eight years of age and to those over this age



the dose must never exceed one-third of a grain daily. The patient should be hospitalized and 1 grain of the drug is given subcutaneously per day for adults on successive days for a period not to exceed eight to 10 days and the course should not be repeated within a shorter interval than one month.

Emetine relieves the acute symptoms in approximately 85 per cent of the cases. However, despite the apparent highly amebicidal property of emetine *in vitro*, it is generally agreed that the alkaloid alone does not result in the cure of amebic infections in more than 10 to 15 per cent of patients. It is relatively efficient in the treatment of liver abscess and amebic hepatitis and at present the only drug available. It should be reserved only for use in the control of the acute symptoms of severe diarrhea and dysentery. Emetine has a direct lethal action on the amebae as demonstrated *in vitro* and is more effective against motile forms than against the cysts. Concentrations of emetine necessary to kill the cystic forms cannot be safely obtained in man.

In therapeutic doses emetine will produce nausea and vomiting when taken by mouth. Emetine frequently causes toxic symptoms, especially noted when its action is cumulative from too high dosage or from prolonged therapeutic use. It is a "general protoplasmic poison," and causes hyperemia, cloudy swelling and cellular degeneration in the liver, heart, kidneys, and skeletal muscles. Emetine as a result of its myotoxic action may produce cardiac arrhythmias and can cause a severe acute degenerative myocarditis which may result in sudden cardiac failure or death. Myositis, muscular weakness, tremors and pain, especially in the arms and legs, and gastrointestinal symptoms are also prominent manifestations of emetine poisoning.

Dack and Moloshok<sup>9</sup> (1947) have recently reviewed a series of 21 cases of amebiasis which were treated with emetine hydrochloride. Nine out of these 21 cases developed toxic cardiac effects with changes in their electrocardiograms. They found that the commonest electrocardiographic abnor-

mality was inversion of the T waves, usually involving all the standard leads. All nine patients in their series showed inversion of the T waves in leads II and III while six showed inversion of the T wave in lead I and 4 in lead IV-F. There was no deviation or depression of the ST segment, but there were abnormalities of the QRS complex in two cases. The duration of the abnormal findings found varied from six weeks to two months or longer. They found, however, that the neuromuscular and gastrointestinal symptoms of emetine poisoning preceded the electrocardiographic changes in the majority of cases. This would lead one to doubt if abnormal changes in the electrocardiogram are in keeping with an early diagnosis of emetine poisoning. They should be taken in every case receiving emetine, however. Earlier Boyd and Scherf<sup>10</sup> (1941) reported similar changes in the electrocardiogram in acute emetine intoxication.

The use of emetine is contraindicated in cases with myocardial, kidney and liver damage. It is also definitely contraindicated in children under eight years of age and is best not used during pregnancy.

*Emetine - Bismuth - Iodide*: DuMez, in 1915, in the Philippine Islands first called the attention of medical practitioners to this compound. It was reported upon favorably by Low and Dale (1916) and by Dobell (1916) as efficient in the treatment of carriers and of patients resistant to emetine alone. This combination is highly regarded by many English authorities who consider it the drug of choice in the treatment of amebic infections.

Emetine-bismuth-iodide contains 29 per cent iodine, 12 per cent bismuth, and 58 per cent emetine. The toxicity of this preparation is essentially that of emetine. The dose of emetine-bismuth-iodide that should be employed is 0.2 gram (3 grains) administered once a day for 21 consecutive days. Rest in bed to prevent or lessen nausea and liability to cardiac failure is recommended. This combination is never used in the United States in the treatment of amebiasis.

*Chiniofon* (anayodin and yatren): This is an iodine compound having the chemical

formula of 7-iodo-8-hydroxyquinolin-5-sulphonic acid and contains 26 to 28 per cent iodine. It was introduced as an amebacide in 1921 by Muhlen and Menk. In therapeutic doses it is non-toxic by mouth or by rectum. Two deaths have been reported from its intravenous use in which liver damage was the outstanding feature.

Chiniofon is prepared in keratin-coated or uncoated pills each containing 4 grains (0.25 gram). Three to four pills (12-14 grains) are given to an adult by mouth three times a day for a period of eight to 10 days. For children one grain per 10 pounds of body weight is given three times a day for approximately the same period of time. Following meals 12 to 16 grains (three or four tablets) are given by mouth for a period of seven days. If no *Endamoeba histolytica* are found in the stools over a period up to six months, no further treatment is necessary. If the stools remain positive, the treatment is repeated following a rest period of at least seven days. The drug may be administered without interfering with the patient's daily routine, and no precautions are necessary regarding diet or exercise except in cases manifesting symptoms.

Chiniofon is an efficient amebacide and has a proved efficacy of approximately 90 per cent or better. It should not be used in the presence of iodine intolerance or liver damage and must be given with caution to patients with thyroid disease.

*Vioform*: Chemically, this compound is iodochlorhydroxyquinoline, containing between 37.5 and 41.5 per cent iodine. It is prepared in the form of gelatin capsules each containing 4 grains (0.25 gram). The dose for adults is 4 grains (one capsule) three times a day for 10 days. Twice this dose is recommended for severe infections. For children the dose is one-third grain per 15 pounds of body weight three times a day for 10 days. The course may be repeated following a rest period of seven days. There is no interference with the patient's daily routine.

In the treatment of amebiasis, vioform has an efficacy of approximately 80 per

cent. It has also been used since its introduction as a substitute for iodoform as a dusting powder for application to wounds, burns, skin eruptions, and so on.

The toxicity of vioform is slight unless therapeutic doses are exceeded. It is considered more toxic than chiniofon but less toxic than carbarsone. Contraindications for its use are essentially the same as for chiniofon.

*Diodoquin*: Chemically, it is an iodine compound in which the sodium sulfonate radical of chiniofon is replaced with a second iodine atom, increasing thereby the iodine content to 63.9 per cent. The drug is prepared in tablets containing 3.2 grains (0.21 gram).

For adults the dose recommended in the treatment of amebiasis is from 22.5 to 30 grains (seven to 10 tablets) daily for a period of two to three weeks. The dose for children consists of one tablet daily per 15 pounds of body weight. The tablets are given in divided doses following meals, and the course may be repeated after a rest period of seven to 10 days.

Diodoquin has been found to be non-toxic in therapeutic doses and only an occasional headache and mild gastrointestinal disturbance if any have been reported from its use. It is considered by most authorities the least toxic of the amebacidal drugs.

Summarizing the clinical results observed in his investigation of the use of diodoquin in the treatment of amebiasis, D'Antoni<sup>11, 12</sup> (1942-43) stated: "On the basis of 126 cases, diodoquin would seem to be more than 92 per cent effective in single cases and 99 per cent effective in all patients treated. No drug previously used in the treatment of amebiasis has given such consistently satisfactory results." The drug has also been reported on very favorably by Hummel<sup>13</sup> (1937-1940) and Almy<sup>14</sup> in this country and by Morton<sup>15</sup> and Manson-Bahr<sup>16</sup> in England.

Manson-Bahr<sup>16</sup> states that diodoquin "is well tolerated. The great advantage of this simple treatment is that in the vast majority, it destroys the cysts of *E. histolytica* and is, therefore, especially valuable in steriliz-



ing 'cyst-carriers.' It can readily be taken by ambulant patients and, therefore, eliminates the necessity of hospitalization."

Craig<sup>1</sup> believes that diodoquin will be of definite value in the prophylactic treatment of amebiasis and that further observations may well demonstrate that it is the most specific drug that we possess for the treatment of this infection.

*Carbarsone*: This drug was first prepared by Ehrlich and is a white crystalline solid without taste or odor, almost insoluble in water but soluble in alkaline aqueous solutions, and contains 28.85 per cent of arsenic. The chemical formula of this compound is 4-carbaminophenylarsonic acid.

Carbarsone is directly amebicidal by virtue of its arsenic content. Anderson and Reed<sup>17</sup> (1931) first introduced this compound as a specific in the treatment of amebiasis. It is more effective than acetarsone and has a therapeutic index eight times higher. Like chiniofon, the action of carbarsone on motile forms, although effective, is not as rapid as that of emetine. Carbarsone does not act on amebae in abscesses of the liver and other organs. The drug is active against cysts.

The adult dose of carbarsone is 0.25 gram (4 grains) taken orally twice a day for 10 days and the course of treatment may be repeated in resistant cases after an interval of 10 days. Carbarsone can also be given rectally as a retention enema and is used in this manner for acute dysentery with motile amebae in the stool or dysentery cases that have proven refractory to the oral administration of the drug. Anderson and Reed<sup>18</sup> (1934) recommend its employment daily for five days at least in the form of retention enemata consisting of 200 c.c. of a 2 per cent sodium bicarbonate solution containing 1 per cent carbarsone. They also recommend that a rapidly acting sedative as sodium amytal be given orally in a dosage of 0.2 grams (3 grains) in order to produce sleep, thus allowing the patient to retain the drug and if the enema is expelled it should be repeated until at least five enemata have been retained.

Carbarsone is absorbed readily after oral

administration and is excreted rather slowly in the urine. Rest periods between courses are therefore imperative to prevent cumulative toxic effects. Carbarsone appears to be one of the most innocuous of the organic arsenicals. Considering the wide use of the drug, few cases of serious poisoning have been reported. Despite the para position of the amino group, serious optic damage is almost unknown but caution should be used in its administration. Skin rashes of varying severity but usually mild, and localized edemas are occasionally observed. Exacerbation of diarrhea, mild nausea and vomiting, and vague abdominal pains may sometimes occur. Its use is contraindicated in the presence of liver and kidney disease.

Reed<sup>18</sup> (1935) is of the opinion that carbarsone is the best of all amebicidal drugs. He administered the drug to 330 patients with amebiasis, only three of whom showed symptoms of intolerance, and the drug was successful in eliminating the infection of 90 per cent of these patients. Craig<sup>1</sup> (1944) believes that carbarsone, in the treatment of carriers and mild infections with *Endamoeba histolytica* may be relied upon to eliminate the infection in from 85 to 95 per cent of the cases, while a repetition of the drug and course of treatment will result in the elimination of most of the resistant infections. However, he believes also that since the drug is an arsenical and more toxic than the iodine preparations, it is generally less useful than the latter and that carbarsone treatment should be reserved for those infections which have proven incurable with the iodine compounds.

*Treparsol*: This drug is an arsenoben-zolic derivative of the salvarsan type and is furnished in tablets containing 0.25 gram (4 grains). It has been used in the treatment of amebic dysentery and amebiasis with good results but it has the disadvantage of the toxicity inherent in all arsenic compounds, although the evidence points to its being less toxic than acetarsone.

The dose of the drug as recommended by Brown<sup>19</sup> of the Mayo Clinic is 0.25 gram (4 grains) three times a day with meals for four days; cessation of the treatment for

ten days; and finally 0.25 gram three times a day for four days. The tablets should be chewed with the food as this causes greater dispersion of the arsenic.

*Acetarsonic*: This compound, which is also known as Stovarsol, was introduced by the French for the treatment of syphilis, and is a synthetic arsenical (acetylaminohydroxyphenylarsonic acid) containing from 27.1 to 27.4 per cent of arsenic. It was formerly extensively used in the treatment of amebiasis and was administered in tablet form by mouth, each tablet containing 0.25 gram (4 grains) of the compound. It is little used today.

#### OTHER DRUGS EMPLOYED IN TREATMENT

The bacterial flora of the intestines has some bearing on the virulence of amebic infection. A purely amebic infection is rare, for every infection is complicated by the presence of pathogenic bacteria which have penetrated into the tissues via lesions produced by the amebae.

Sokoloff<sup>20</sup> (1945) has demonstrated that the virulence of *Endamoeba histolytica* may be increased when it is inoculated along with certain bacteria into experimental animals. He found that streptococci and staphylococci apparently enhance the multiplication of *Endamoeba histolytica*; that *Clostridium perfringens* (of the *B. welchii* group) and *Lactobacillus acidophilus* induce the encystment and coagulation of the free-living amebae.

Many of such cases complicated by secondary bacterial invasion do not respond favorably to specific anti-amebic therapy and tend to become chronic. It has been found that by combating the bacterial infection present in the colon and following this with amebicidal therapy that many of the so-called "resistant" or chronic forms of the infection can be treated successfully. Three or four of such therapeutic agents will be briefly discussed below.

*Succinylsulfathiazole*: Little information has as yet been published on the use of sulfonamides or of penicillin to combat secondary bacterial infection in amebiasis. However, marked benefit has been reported by Hargreaves<sup>21</sup> (1945) in severe amebic

infection following the administration of sulfasuxidine (succinylsulfathiazole) by mouth in conjunction with penicillin intramuscularly and he has seen marked improvement after the use of penicillin alone. The total dosage recommended by Hargreaves was 80 grams given in divided doses of 1 gram every three to four hours. A standard course of anti-amebic treatment was given after completion of the antibacterial therapy.

*Penicillin*: As already mentioned in the preceding discussion, penicillin has proved to be a very useful adjunct in the treatment of chronic cases of amebic colitis by virtue of its ability to combat secondary bacterial infection. In addition to Hargreaves another English writer, Willmore<sup>22</sup> (1945), reports similar experiences with penicillin.

Hargreaves and Willmore recommended an initial injection of 100,000 units of penicillin intramuscularly to be followed by 33,000 units at three-hourly intervals with a total dosage of two million units.

*Trilactic* is the anhydrous form of lactic acid which dissolves slowly in water, decreases the pH of the large intestine, and promotes the growth of acidophilic bacteria. There is some indication that as a general rule bacteria which lower the pH inhibit the multiplication of amebae. *In vitro* experiments carried out at the University of California by Sokoloff<sup>20</sup> and Kessel (1945) have demonstrated a definite antibiotic action of lactic acid. They found that lactic acid causes coagulation of almost all amebae in cultures within 30 minutes in concentrations of 0.0098; changes in the nucleus of amebae and arrested motility; and that the mode of action may be on the amylase which is present in large quantities in the body of all amebae.

Trilactic was given by Sokoloff to 62 patients affected with acute and chronic amebic infections in the form of the anhydrous form of lactic acid. For the acute dysentery 40 to 50 grams of trilactic were given daily in divided doses of four and given in pulverized rice or semi-fluid oatmeal for seven days and then gradually decreased after the acute stage was arrested. For chronic



amebiasis without dysentery three to four tablespoons daily divided into two doses, morning and at night were given. In 34 cases, or in 54 per cent, complete recovery was noted. In 19 per cent results were negative. In the remaining cases considerable improvement was observed. This is an entirely new form of anti-amebic therapy and demands more extensive clinical trial before a clear evaluation can be made of its amebicidal properties.

*Kurchi Bark*: The bark of a deciduous tree (*Holarrhena antidysenterica*) which is a native of the tropical Himalayas, has for many years had a reputation among the natives of India and adjacent regions as a remedy in diarrhea and dysenteries. The chemical composition of the bark has been thoroughly studied and several alkaloids have been isolated. At the present time the presence of four alkaloids in the bark of this tree has been demonstrated, that is, conessine, holarrhenine, kurchicine and kurchine, the latter occurring in the largest amount. The favorable results obtained in the treatment of amebiasis with this substance is due to a direct action on the amebae.

At the present time Kurchi-bismuthiodide has largely replaced the administration of the total alkaloids by intramuscular injection, but the total alkaloids may be administered orally in the form of the standard fluid extract of kurchi bark, which contains about 0.032 gram ( $\frac{1}{2}$  grain) of the alkaloids in 4 c.c. The dose of the extract is 8 c.c. three times a day for as long as four to six weeks in chronic infections. The dose of kurchi-bismuthiodide varies from 0.25 gram (4 grains) orally twice a day for 10 days in chronic amebic infections to as much as 0.65 gram (10 grains) twice a day for 10 days in severe amebic infections.

*Bismuth Subnitrate*: For many years bismuth subnitrate has been used in the treatment of amebic dysentery. The drug alone was used for a while but has since been combined with emetine and this combined method is still in use by some today in the treatment of amebiasis. The subni-

trate of bismuth acts by its antiseptic properties upon the bacteria of the intestine, reducing putrefaction, thus indirectly producing degenerative changes in the ameba because of this change in the environment of the organisms. In order for the drug to be effective it must be given in very large doses. A heaping teaspoonful, equivalent to about 180 grains in weight, mechanically suspended in almost a tumbler full of plain, or better, effervescent water, or in milk, is given every three hours day and night, lessening the amount only when improvement occurs.

*Shadocol*: Chemically, this drug is sodium tetraiodophenolphthalein (also called opacol and T.I.P.). The acidic form is prepared for oral administration as a suspension of the white acid body which is turned into the blue soluble sodium salt in the intestinal canal. The dye is absorbed from the intestinal canal, secreted by the liver, and excreted with the bile. One-half bottle of the dye is given to children under 6 years of age and all over this age are given one full bottle of the dye. A saline cathartic is given the next morning. No special dietetic measures and no other medication is employed with the dye.

Alexander, Park-Ross, and Stein<sup>23</sup> (1944) from South Africa reported 74 per cent sterilization of the intestinal canal following the administration of the shadocol in the treatment of amebiasis, based on immediate stool examinations. The follow-up on this drug is not too encouraging but results in their hands have been uniformly good.

#### TREATMENT OF AMEBIASIS

The treatment of amebiasis embraces the treatment of carriers and mild infections; amebic enteritis and amebic dysentery; amebic abscess of the liver, and other complications of this infection. However, it must be stated that at the present time we do not possess a *single* drug that will eliminate the amebic infection in *every* case. It is hoped that with further research and investigation in this field that a specific amebicide will be developed which will

eliminate the infection with *Endamoeba histolytica* in every case.

#### THE TREATMENT OF SYMPTOMLESS CARRIERS AND MILD INFECTIONS

It is agreed by most authorities today that in the treatment of carriers and mild infections chiniofon is usually the drug of choice. It is supplied in pills or tablets, each containing 0.25 gram (4 grains), and the dose for an adult is three tablets or pills given three times a day for a period of eight to 10 days. The full dose sometimes causes diarrhea so that it is well to commence with a smaller dose and increase it as it is well tolerated. Chiniofon is not a toxic drug and may be used safely in mass therapy and the treatment does not interfere with the occupation of the patient. In treating children the dose of chiniofon should be governed according to age and general condition.

One course of eight to 10 days with chiniofon is usually successful in eliminating *Endamoeba histolytica* in carriers and mild symptomatic infections but if not, the course should be repeated after an interval of 10 days.

In view of the very favorable reports upon diodoquin, Hummel,<sup>13</sup> D'Antoni<sup>11, 12</sup> and Morton,<sup>15</sup> it is felt that this compound will be equally efficient in such infections and, as it does not produce diarrhea, may be preferable, especially in children. For adults the dose recommended for oral administration is two tablets, each containing 0.21 gram (3.2 grains) three times a day for a period of 20 days. The dose for children consists of one tablet daily per 15 pounds of body weight.

If treatment with either of these compounds does not result in a cure, a course of treatment with carbarsone should be followed, 0.65 gram (4 grains) of this compound being administered twice daily, after the morning and evening meals, for a period of 10 days.

#### THE TREATMENT OF AMEBIC DIARRHEA OR ENTERITIS

If the patient is seen during an attack of severe diarrhea, rest in bed is indicated, and the administration of chiniofon as already described but beginning with not more than two pills three times a day for an adult.

The number of pills may be increased progressively with improvement in the symptoms. If the diarrhea is particularly severe, it is sometimes wise to administer emetine hydrochloride subcutaneously in doses not to exceed 0.065 gram (1 grain) a day for not more than six to seven days, after which chiniofon should be administered as recommended.

If the patient is seen between diarrheal attacks, the treatment in such cases conforms very much to that as already described for carriers. Then, too, if there is a history of recurrent bouts of severe diarrhea, it may be necessary to repeat the course of treatment with chiniofon after a rest period of about 10 days until the infection is eliminated.

Diodoquin is highly recommended also for the treatment of amebic diarrhea or enteritis in dosages as already outlined. If neither chiniofon nor diodoquin is successful in combating the infection, a course of carbarsone should be given as already recommended in the treatment of carriers and mild symptomatic infections.

Care should be taken with regard to the diet in cases of amebic diarrhea. It should be fluid or semifluid in character and limited to substances that are easily digested.

#### THE TREATMENT OF ACUTE DYSENTERY

Bed rest is absolutely essential for patients with symptoms of acute dysentery. The acute symptoms can be controlled with one grain (0.065 gram) of emetine hydrochloride given subcutaneously once a day until symptoms subside but not to exceed 12 grains, or even better never to administer it for more than 10 days. *It should be emphasized that emetine hydrochloride is to be employed only to control the acute dysenteric symptoms.*

After the dysenteric symptoms are controlled with emetine, a standard course of chiniofon or diodoquin is administered as in the treatment of carriers and those presenting symptoms of enteritis. If either of these drugs fails, a full course of carbarsone or vioform is recommended.

D'Antoni<sup>24</sup> recommends that neoprontosil



or some other intestinal antiseptic be administered in conjunction with the chiniofon or diodoquin to combat any secondary bacterial infection that may be present.

The English<sup>21</sup> recommend the use of emetine hydrochloride subcutaneously in one grain daily until the dysenteric symptoms are relieved, not to exceed 10 days, followed by emetine-bismuth-iodide orally in the dose of three grains per day for 12 consecutive days. In severe cases this may be combined with daily retention enemata of chiniofon.

To secure the best results with chiniofon alone in the treatment of acute amebic dysentery, the use of high enemata containing chiniofon should be combined with treatment by mouth. When this is done, it is recommended that chiniofon be given by mouth in doses not to exceed 0.5 gram (7.5 grains) three times a day and daily enemas, best given at night, consisting of 200 c.c. of a 2 per cent warm water solution of chiniofon and retained for several hours if possible.

Routine stool examinations should be made after the disappearance of symptoms and the treatment with chiniofon or diodoquin repeated if they are found positive for *Endamoeba histolytica*.

#### THE TREATMENT OF CHRONIC AMEBIC DYSENTERY

There is a great difference of opinion regarding the best method for the treatment of chronic amebic dysentery. In general, however, the treatment of this condition depends upon whether the patient is seen during an acute exacerbation of the dysenteric symptoms or between the dysenteric attacks.

In this country if the patient is seen during an acute exacerbation, most authorities recommend the treatment of the acute symptoms as already described for acute amebic dysentery, while if the patient is seen during a quiescent period he should be given a course of chiniofon, diodoquin, or carbarsone, if the stools contain the amebae, in the manner already described. It is absolutely necessary for patients to be confined to bed during an acute exacerbation. Good nursing care and a proper diet are also absolute essentials.

Hargreaves<sup>21</sup> in England (1945) outlined

the standard treatment employed in the treatment of Service Personnel with chronic amebic dysentery. It consisted of a 12 day course of emetine-bismuth-iodide together with daily retention enemata of chiniofon (200 c.c. of a 2.5 to 5 per cent solution at body temperature). This was followed by a course of carbarsone, four grains twice daily for 12 days. If the patient had dysenteric symptoms, this course was preceded by six daily injections of emetine hydrochloride of one grain each subcutaneously. Secondary bacterial invaders were controlled in severe cases by the use of penicillin and sulfasuxidine.

In contrast to the above method of treating chronic amebiasis Adams<sup>25</sup> at the Liverpool School of Tropical Medicine has advocated a 21 day "blunderbuss" therapy which includes the following: (1) Emetine as aurementine by mouth in doses of one grain three times a day in capsules on odd numbered days; (2) stovarsol or carbarsone in doses of 4 grains three times a day on even numbered days with a retention enema of 8 to 15 oz. of freshly prepared 2½ per cent quinoxyl in the evening, changing to a 4 per cent solution halfway through the course; (3) bismuth subnitrate in doses of 60 grains three times a day in milk to be given every day; (4) the retention enema is preceded by a rectal wash-out with a weak solution of sodium bicarbonate solution to remove the mucous.

A series of 80 cases were studied using the two different methods outlined by Hargreaves and Adams, dividing the cases equally. Out of the 40 cases tried on the Standard Treatment advocated by Hargreaves only six (or 15 per cent) were not cured; of the 40 cases tried on the Liverpool 21 day "blunderbuss" treatment 21 cases (or 52 per cent) were not cured.

#### TREATMENT OF COMPLICATIONS OF AMEBIASIS

According to Craig,<sup>1</sup> the most important of the complications of amebiasis are amebic hepatitis, amebic abscess of the liver and amebic abscess of the lung.

The treatment of amebic abscess of the liver and of the lung is largely a surgical problem, but the early recognition of amebic hepatitis and beginning abscess formation

is essentially a medical problem. The only drug effective in the treatment of such extraintestinal lesions of amebiasis is emetine hydrochloride. For the treatment of extraintestinal amebiasis, emetine hydrochloride is given in doses of 1 grain daily subcutaneously for a period not to exceed 10 days. It should not be repeated in less than a month.

Sodeman and Lewis<sup>26</sup> (1945) in a review of the last 33 cases of amebic hepatitis seen at the New Orleans Charity Hospital and the U. S. Marine Hospital at New Orleans concluded that early diagnosis led to effective treatment with emetine alone in many cases. Even at times when known abscess occurs treatment with emetine alone may be successful according to Hodson (1921).

#### CRITERIA FOR CURE

The treatment of amebiasis, particularly the dysenteric phases, is governed chiefly by stool examinations for *Endamoeba histolytica*. After each course of therapy stool examinations should be made and if positive for *Endamoeba histolytica* the treatment should be repeated. Craig<sup>1</sup> believes that at least three negative microscopic examinations of the stools, one week apart, should be secured before the patient is considered cured and thereafter, for at least three months, the examination of the stool should be repeated once a month.

However, it is my firm belief that a set criteria for cure cannot be established rigidly. One reason for this statement is the very evident fact that it is impossible to determine whether a patient has a relapse or a reinfection if the *Endamoeba histolytica* are found in the stools two weeks to three months after treatment. Therefore, it would seem advisable not to regard a particular amebacidal drug as an ineffective amebicide too hastily on this particular basis just because the trophozoites of cysts of *Endamoeba histolytica* reappear in the feces after specific treatment. It is a definite fact that there is no one drug or method of treatment which will cure every case of amebiasis today. It is hoped that with continued research and investigation in the field an effective, non-toxic amebicide will

be discovered which will eliminate the infection in every case.

#### CONCLUSIONS

1. Amebiasis has been found in the United States wherever surveys have been conducted and the disease can no longer be properly referred to as a "tropical disease" *per se*.

2. Emetine is very effective in the treatment and control of the acute and severe symptoms of intestinal amebiasis, but clinical results are sufficient to prove that emetine hydrochloride does not, even when given in repeated courses of 12 grains with doses of 1 grain daily, cure many cases of endamebic dysentery, if by cure is meant the destruction of cysts in the majority of cases.

3. Emetine is the only drug available at the present time for the treatment of extraintestinal amebiasis and such complications of intestinal amebiasis as ameboma.

4. At the present time the drug of choice for the treatment of intestinal amebiasis is chiniofon. In therapeutic doses it is non-toxic by mouth or by rectum and is efficient in 90 per cent or more of the cases of amebiasis.

5. Diodoquin appears to be equally as effective as chiniofon in the treatment of intestinal amebiasis and, as it does not produce diarrhea following its administration, may be preferable, especially in children. However, it will be necessary to observe more cases treated with diodoquin before a true evaluation of its efficiency can be firmly established.

6. At the present time we do not possess a single drug that will eliminate the amebic infection in every case. It is hoped that with further research in this field a specific amebicide will be developed which will eliminate the infection with *Endamoeba histolytica* in every case.

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## PREMATURITY—AN ORIENTATION\*

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Premature births constitute at least 5 per cent of the total births in the United States. This means that at least 150,000

premature infants were born in 1944. The proportion is probably considerably higher than this if a birth weight of 2,500 gm. or less is used as the criterion of prematurity. In New York City 7.3 per cent of the nearly 100,000 infants born in 1939 were premature on this basis.

It is necessary for clinical and for statistical purposes, to have a definite and objective delimitation between a premature and a mature infant. There is general agreement that a birth weight of 2,500 gm. or less is the best criterion for prematurity based on clinical indications of the need for special care and, in addition, on the sharp contrast in mortality among infants above and below this birth weight. In this connection Eastman<sup>1</sup> found that in the Johns Hopkins Hospital the fatality rate (percentage of deaths among infants in specified weight groups, born alive at the hospital) was 0.4 per cent among mature infants (those weighing at birth 2,500 gm. or more), whereas among premature infants (those weighing 1,000 to 2,500 gm.) it was 10.7 per cent. Even among infants on the borderline of maturity (those weighing 2,000 to 2,500 gm.) the fatality rate was 4.2 per cent—ten times that for mature infants. These figures apply to the period 1941-45.

The question has been raised of setting a low birth-weight limit for differentiation between abortions and premature live births. This is, however, more difficult than that of setting the upper limit of birth weight, since gestation period and birth weight are usually not closely correlated. In addition, infants have survived and grown to normal childhood whose gestation period or birth weight placed them in the "non-viable" obstetric classification. There are reports of the survival of a fairly large number of infants who weighed at birth less than two pounds and of a few who weighed less than one pound. The American Academy of Pediatrics recommends that all *live-born* infants weighing 2,500 gm. or less at birth should be classified as premature.

\*Presented before a meeting of the New Orleans Post-graduate Medical Assembly, February 24, 1947.

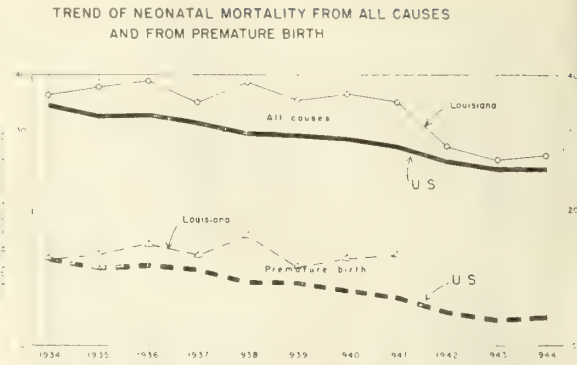
This brief orientation is made chiefly to point up the high mortality from prema-

ture birth and the chief causes thereof as well as the chances for reducing this mortality and the prognosis for future development of these infants.

NEONATAL MORTALITY FROM PREMATURE BIRTH

The mortality rates for the United States birth-registration area are compiled from data on death certificates that show prematurity as the primary cause of death. Deaths of premature infants recorded as due to birth injury or congenital defect are classified by the Bureau of the Census in these latter cause groups according to the rules of the International List of Causes of Death.

The trend of the neonatal mortality rates from all causes and from premature birth in the past 11 years for the United States



and for Louisiana are shown in figure 1.\* The downward trends are apparent, as is the fact that the rates for Louisiana are considerably higher than those for the United States. Tables 1a and 1b show the figures on which these trends are based.

TABLE 1a  
NEONATAL MORTALITY FROM ALL CAUSES AND FROM PREMATURE BIRTH; UNITED STATES, 1934-44

Deaths in the first month from—					
All causes			Premature birth		
Year	Number of live births	Number	Rate per 1,000 live births	Number	Rate per 1,000 live births
1944	2,794,800	68,996	24.7	32,065	11.5
1943	2,934,860	72,632	24.7	33,513	11.4
1942	2,808,996	72,122	25.7	33,483	11.9
1941	2,513,427	69,559	27.7	32,278	12.8
1940	2,360,399	67,866	28.8	31,437	13.3
1939	2,265,588	66,383	29.3	31,260	13.8
1938	2,286,962	67,735	29.6	31,582	13.8
1937	2,203,337	68,887	31.3	32,524	14.8
1936	2,144,790	69,869	32.6	32,452	15.1
1935	2,155,105	69,834	32.4	32,021	14.9
1934	2,167,636	73,841	34.1	33,802	15.6

Based on data from U. S. Bureau of the Census for continental United States.

TABLE 1b  
NEONATAL MORTALITY FROM ALL CAUSES AND FROM PREMATURE BIRTH; LOUISIANA, 1934-44\*

Deaths in the first month from—					
All causes			Premature birth		
Year	Number of live births	Number	Rate per 1,000 live births	Number	Rate per 1,000 live births
1944	61,050	1,654	27.1	857	14.0
1943	62,005	1,651	26.6	†	†
1942	58,093	1,639	28.2	†	†
1941	54,618	1,931	35.4	929	17.0
1940	50,916	1,869	36.7	853	16.8
1939	48,844	1,738	35.6	775	15.9
1938	48,867	1,883	38.5	891	18.2
1937	46,006	1,622	35.3	778	16.9
1936	43,828	1,703	38.9	773	17.6
1935	42,270	1,600	37.9	716	16.9
1934	43,002	1,567	36.4	716	16.7

\*1934-40, by place of occurrence; 1941-44, by place of residence.

†Not available.

Based on data from U. S. Bureau of the Census.



TREND OF NEONATAL MORTALITY FROM PREMATURE BIRTH, BY RACE

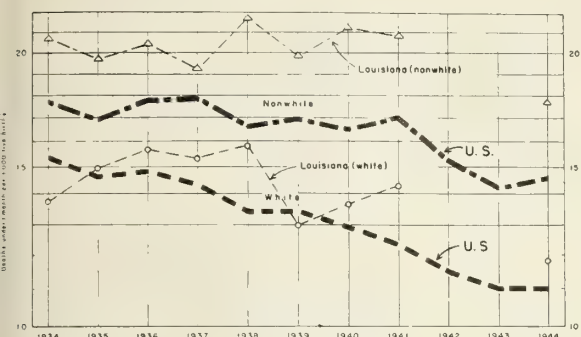


Figure 2 shows the neonatal rates by race for the same period. The downward trend in the United States is apparent for both white and non-white premature in-

fants. In Louisiana the trend in the mortality rate for white infants was irregular, and the rate in 1944 was somewhat higher than that for the United States. The Louisiana rate for non-white infants was maintained at a much higher level than the rate for the United States in the entire period 1934 to 1944. In 1944 there was a considerable decrease, however, in the Louisiana rate for non-white infants, but it was still much higher than that for the United States. The figures on which these trends are based are shown in tables 2a and 2b.

\*Charts and tables based on Census Bureau data prepared by Children's Bureau, Social Security Administration, Federal Security Agency.

TABLE 2a

NEONATAL DEATHS FROM PREMATURE BIRTH, WHITE AND NON-WHITE; UNITED STATES, 1934-44

Year	Number of live births		Deaths in the first month from premature birth			
	White	Non-white	Number		Rate per 1,000 live births	
			White	Non-white	White	Non-white
1944	2,454,700	340,100	27,109	4,956	11.0	14.6
1943	2,594,763	340,097	28,670	4,843	11.0	14.2
1942	2,486,934	322,062	28,588	4,895	11.5	15.2
1941	2,204,903	308,524	27,034	5,244	12.3	17.0
1940	2,067,953	292,446	26,620	4,817	12.9	16.5
1939	1,982,671	282,917	26,491	4,769	13.4	16.9
1938	2,005,955	281,007	26,905	4,677	13.4	16.6
1937	1,928,437	274,900	27,635	4,889	14.3	17.8
1936	1,881,883	262,907	27,786	4,666	14.8	17.7
1935	1,888,012	267,093	27,513	4,508	14.6	16.9
1934	1,866,231	301,405	28,480	5,322	15.3	17.7

Based on data from U. S. Bureau of the Census for continental United States.

TABLE 2b

NEONATAL MORTALITY FROM PREMATURE BIRTH, WHITE AND NON-WHITE; LOUISIANA, 1934-44\*

Year	Number of live births		Deaths in the first month from premature birth			
	White	Non-white	Number		Rate per 1,000 live births	
			White	Non-white	White	Non-white
1944	37,463	23,587	441	416	11.8	17.6
1943	38,392	23,613	†	†	†	†
1942	35,082	23,011	†	†	†	†
1941	32,207	22,411	460	469	14.3	20.9
1940	29,853	21,063	408	445	13.7	21.1
1939	28,567	20,277	371	404	13.0	19.9
1938	28,684	20,183	454	437	15.8	21.7
1937	26,534	19,472	407	371	15.3	19.1
1936	25,376	18,452	396	377	15.6	20.4
1935	24,417	17,853	364	352	14.9	19.7
1934	24,877	18,126	340	376	13.7	20.7

\*1934-40, by place of occurrence; 1941-44, by place of residence.

†Not available.

Based on data from U. S. Bureau of the Census.

These Census Bureau figures give evidence of decreased neonatal mortality from premature birth. Hospital fatality rates also offer some evidence that improved meth-

ods of diagnosis and treatment, as well as general care of these infants, have been effective in saving lives.

Table 3, showing the range in fatality

TABLE 3  
RANGE IN HOSPITAL FATALITY RATES IN EARLIER AND LATER PERIODS

Period	Total 2,500 gm. or less	Fatality rate			
		Less than 1,000 gm.	1,000- 1,500 gm.	1,501- 2,000 gm.	2,001- 2,500 gm.
Earlier period (11 hos- pitals, 1922-40)	15.9-32.0	87.5-100.0	50.0-82.5	17.4-45.6	3.9-15.9
Later period (6 hos- pitals, 1940-45)	15.0-27.4	85.0-100.0	41.4-55.4	12.8-30.5	3.7-7.9

rates of premature infants by birth-weight groups, is based on reports from 11 hospitals with 9,711 cases during varying periods from 1922 to 1940 and on reports from six hospitals with 5,126 cases during varying periods from 1940 to 1945. It can be seen that in all weight groups except the lowest, both lowest and highest rates were lower in the later than in the earlier period. These lowered rates were reported by hospitals in which some special efforts have been made to improve methods of care. In

most hospitals the country over the fatality rates are not so favorable as those shown in this table.

CAUSES OF DEATH AMONG PREMATURE INFANTS

Figure 3 shows the causes of neonatal deaths in the United States for 1944 and table 4 gives the corresponding information for Louisiana. Premature birth, as in every year, holds first place, accounting for almost half of these deaths. Some of these premature infants died because they were

CAUSES OF DEATH IN FIRST MONTH OF LIFE  
UNITED STATES, 1944

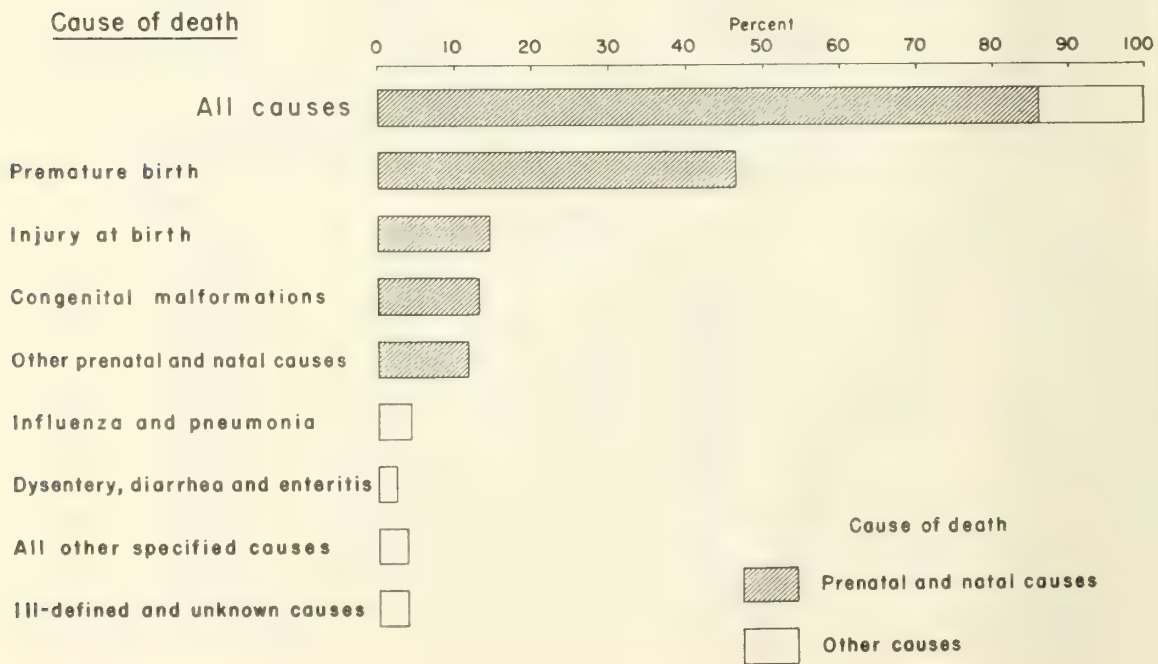




TABLE 4

CAUSES OF DEATH IN FIRST MONTH OF LIFE; LOUISIANA, 1944

Cause of death (Numbers in parenthesis are those of the International List of Causes of Death)	Number of deaths	Per cent distribution	Rate per 1,000 live births
All causes	1,654	100.0	27.1
Premature birth (159)	857	51.8	14.0
Injury at birth (160)	217	13.1	3.6
Congenital malformations (157)	119	7.2	1.9
Other prenatal and natal causes	210	12.7	3.4
Congenital debility (158)	27	1.6	0.4
Other diseases peculiar to the first year of life (161)*	149	9.0	2.4
Syphilis (30)	34	2.1	0.6
Influenza and pneumonia (33, 107-109)	88	5.3	1.4
Dysentery, diarrhea and enteritis (27, 119)	24	1.5	0.4
All other specified causes	92	5.6	1.5
Ill-defined and unknown causes (199, 200)	47	2.8	0.8

\*That occurred in the first month.

Based on data from U. S. Bureau of the Census (Louisiana Summary of Vital Statistics 1944).

too immature for extra-uterine existence. Some died because of conditions associated with birth; anoxia, birth trauma, or congenital malformations not diagnosed. Some died because they received inadequate care: that is, they were unnecessarily exposed to infections, lived under unsuitable environmental conditions, were improperly fed, or

were improperly or inadequately treated when they became ill.

An indication of the relative importance of the various causes of death of premature infants is obtained from study of the proportion of these infants that died at various ages. The data for the United States and for Louisiana in 1944 are shown in table 5.

TABLE 5

NEONATAL MORTALITY FROM PREMATURE BIRTH, BY AGE; UNITED STATES AND LOUISIANA, 1944

Age at death	United States		Louisiana	
	Number of deaths	Per cent	Number of deaths	Per cent
Under one month	32,065	100.0	857	100.0
Under one day	18,909	59.0	477	55.7
One day to six days	9,750	30.4	237	27.6
One week to three weeks	3,406	10.6	143	16.7

More than half of the deaths of premature infants occurred on the first day both in the United States as a whole and in Louisiana. These deaths can be reduced: (1) by the use of analgesics and anesthetics for women in labor that will not result in fetal anoxia; (2) by methods of resuscitation suitable to these small delicate infants; (3) by conservation of the infants' body heat and administration of oxygen.

Both in the country as a whole and in Louisiana more than one-fourth of the

deaths occurred from the second to the seventh day. These deaths can be reduced by providing: (1) skilled medical and nursing care; (2) suitable environmental conditions—temperature, humidity, ventilation, increased oxygen, and protection from infection; (3) suitable feeding and fluids; and (4) appropriate treatment for diseases peculiar to these first days of life.

In the third period, from the end of the first week to the end of the first month, occurred only 11 per cent of the deaths in

the United States but 17 per cent of those in Louisiana. Deaths in this period are due largely to infection, and these are preventable.

The proportion of deaths of premature infants that occur between the end of the neonatal period and the end of the first year is very small.

In addition to improvement in methods for the diagnosis and treatment of abnormal conditions in the infants, *prevention* of premature labor or prolongation of pregnancy until the fetus weighs at least 1,500 gm. (always with consideration of the mother's welfare, of course) will do much to reduce morbidity and mortality from premature birth.

#### INCIDENCE AND PREVENTION OF PREMATURE BIRTH

Adequate prenatal care plays an important role both in the incidence of premature birth and in the proportion of premature infants who die. Parmelee<sup>2</sup> has shown that in a large series of hospital maternity cases only 5.2 per cent of the infants were premature among the mothers who were healthy, but 8.4 per cent were premature among the mothers who had medical complications. Of the infants of healthy mothers only 1.8 per cent died, compared with 3.5 per cent of the infants of mothers with complications.

Beck<sup>3</sup> has given careful consideration to this aspect of prevention of prematurity. He found, for example, that although for some women with cardiac conditions, pregnancy should not be risked, others may be brought safely to term with proper treatment. He stresses the importance of cardiology consultation service through pregnancy for these cases. The danger of heart failure is greatest in the eighth month of pregnancy, according to Carr and Hamilton.<sup>4</sup> White<sup>5</sup> has found in her studies of diabetic women that premature births were reduced from 40 to 15 per cent when treatment to correct hormonal imbalance (estrogen and progesterone) was combined with insulin therapy.

Syphilis is known to be a cause of premature birth, and in these cases premature

birth is preventable by early and adequate treatment of the mother.

In regard to *obstetric complications* of pregnancy, Anderson, Brown, and Lyon<sup>6</sup> have shown that statistically certain obstetric complications such as toxemia are not *per se* causes of premature labor, but antepartum bleeding was definitely associated with low birth weight. However, in comparing the incidence of each complication in mothers of mature infants and in mothers of premature infants, the authors did not take into consideration in this preliminary report either the severity of the complication or its relation to induced labor. Obviously when labor is induced or operative delivery is undertaken prematurely to save the mother's life, the complication must be considered the cause of the premature birth. As is brought out by Beck,<sup>3</sup> severe toxemia and eclampsia, with which premature birth is most frequently associated, usually do not occur when early and adequate prenatal care is given with due regard to the mother's diet and rest.

There are, unfortunately, a fairly large proportion of premature births for which no cause is determined. In this category such factors as poor nutrition, overwork, emotional disturbances, and so forth, may play a role. Information is scanty because medical histories do not usually record such items. A number of statistical studies of the quality of maternal diet in relation to the incidence of premature birth have shown that the incidence is highest when the diet is poor; lowest when the diet is "good." The incidence of prematurity has been found to be related also to economic status. It is higher among negroes than among whites and higher among hospital ward patients than among private patients. These differences may be related, of course, to poorer environmental conditions, poorer diets, harder work, and more illness among the lower than among the higher economic groups.

#### PROGNOSIS

Finally the evidence must be weighed not only as to the premature infant's chances of



survival but as to his chances for normal growth and development.

Speaking in terms of survival rates rather than fatality rates, table 6 shows the expected survival rates based on a mean between the low and the high rates report-

ed (1940-1945) by five hospitals, giving a better than average grade of care. It can be seen that in the birth-weight group less than 1,000 gm. only a small proportion of the infants can be expected to survive. In the highest birth-weight group (2,001-2-500

TABLE 6

PREMATURE INFANTS: FATALITY AND SURVIVAL RATES; 5 HOSPITALS — 4,737 CASES

Birth weight gm.	Fatality rate		Estimated survival rate
	Lowest	Highest	
Less than 1,000	85.0	100.0	8.0
1,000 - 1,500	41.4	55.4	52.0
1,501 - 2,000	12.8	30.5	78.0
2,001 - 2,500	3.7	7.9	94.0
Total	15.0	27.4	79.0

gm.) 94 per cent should be expected to survive. It is particularly significant that the survival rate is so high in the two intermediate groups (52 and 78 per cent respectively).

Data on physical growth, compiled on measurements of North American premature infants, are meager and not entirely satisfactory, particularly for infants in the lowest birth-weight group. Studies of growth in the first few months of life confirm the findings in earlier European studies that the fetal rate of growth is not interfered with by birth except temporarily. The rate of growth is greater the more immature the infant. Comparisons of weight and height of premature with mature infants must be corrected for conceptional age.

In regard to later growth the studies of Mohr and Bartelme<sup>7</sup> made in Hess' clinic in Chicago, show that the premature infant tends to catch up in weight and length with his siblings at some time near the end of the first to the fourth year or later depending on the degree of prematurity.

In regard to mental development of the premature infant, the studies of Mohr and Bartelme<sup>7</sup> based on relatively large numbers of premature infants and those of Gesell<sup>8</sup> based on long-term studies of individual infants show that premature infants who do not suffer from intracranial injury compare favorably with full-term infants. Mohr and Bartelme<sup>7</sup> found that "those children whose birth weight was low apparent-

ly developed mentally equally as well as those of heavier birth weight." Mental development also must be correlated with conceptional rather than chronologic age up to the time at which the premature infant attains maturity.

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## HOARSENESS\*

## ITS POSSIBLE IMPLICATIONS AND ITS PROPER MANAGEMENT

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NEW ORLEANS

One morning recently, at an otolaryngologic operative clinic at Charity Hospital

\*Read before the Sixty-seventh Annual Meeting of the Louisiana State Medical Society, New Orleans, May 14, 1947.

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of Louisiana at New Orleans, four patients were seen with possible carcinoma of the larynx. Biopsy was positive in three of the four cases. In all three of the positive cases the disease was inoperable. In all four cases the patient's history included the statement that some time before—usually a fairly long time before—there had occurred some alteration in his voice to which he had paid no attention.

It must be granted that the striking combination of circumstances just described is not usual. One seldom sees in the course of a few hours three patients with proved carcinoma of the larynx. But the rest of the story is not at all unusual. It is, in fact, a sad commonplace. Hoarseness is almost always the first symptom of carcinoma of the larynx. Hoarseness is almost always ignored by the patient for longer or shorter periods of time. In too many instances, if he does seek medical advice, hoarseness, which is a symptom only, is treated as if it were a disease. And the end-result is that most patients with carcinoma of the larynx are beyond salvage when they are first seen by the otolaryngologist.

If proof of these statements is needed, statistics from the New Orleans Charity Hospital supply it. Carcinoma of the larynx begins in perhaps 80 per cent of all cases on the anterior half of the vocal cord. In this location it promptly interferes with approximation or vibration of the cord and disturbances of the voice occur correspondingly promptly. The majority of malignant neoplasms of the larynx are squamous-cell and therefore slow-growing. Metastases occur late because lymphatic drainage of the anterior half of the larynx is scanty. The circumstances in carcinoma of the larynx are thus highly favorable for cure, and complete removal of the growth with a margin of healthy tissue is possible in most cases which are seen early. Yet at the New Orleans Charity Hospital, over the two year period ending June 30, 1946, 13 tracheotomies were performed in carcinoma of the larynx, against no laryngectomies and laryngofissures. In the face of these proportions it is scarcely necessary to dwell

further on the gloomy picture of this disease in an indigent hospital population, though it might be well to add that the experience in private practice is often almost equally gloomy. It also seems unnecessary to offer an apology, or even to present an explanation, for these remarks on hoarseness.

#### ETIOLOGIC CONSIDERATIONS

How important a symptom hoarseness may be is evident in the recent comprehensive article by Frank.<sup>1</sup> Defining hoarseness as any alteration in the speaking voice which gives it a rough or rasping character—a definition in which we concur—he lists 12 separate categories and 96 separate diseases and conditions which may give rise to it. The list, on the surface, is very complete. Whoever reads it, however, could with very little effort add several other etiologic possibilities.

Hoarseness may be the residuum, in colloquial language the hangover of a common cold. It may be the first symptom of an extrinsic and potentially serious condition such as aneurysm of the aorta or the subclavian artery, or a tumor of the pons or medulla, or the so-called syndrome of the jugular foramen. These conditions are admittedly unusual, but any one of them may occur, as any other rare disease may occur, in the case immediately under consideration, and they should always be borne in mind as possibilities. In fact, an experienced otolaryngologist could do worse than keep Frank's comprehensive list under the glass on his desk, while the general practitioner, to whom this plea is chiefly addressed, would profit even more greatly by the reminder.

To speak generally, hoarseness usually occurs under certain special circumstances which may be roughly classified as: (1) voice strain; (2) acute inflammatory and infectious conditions; (3) tuberculosis; (4) syphilis; and (5) neoplasms.

Most of these conditions need no special discussion, though a word or two of comment will perhaps be useful about certain of them. Voice strain, for instance, is not limited to singers, public speakers, teachers,



auctioneers and street hawkers. It also occurs in persons in constant association with deaf persons who do not use hearing aids. Children or adolescents suffering from hoarseness ought to be questioned about their attendance at football games and similar sports, where misuse of the voice is almost contagious. Even an adult who habitually attends baseball games sometimes provides the clue to his own disability when he contributes that information: There are such things as screamer's nodes as well as singer's nodes.

In this connection it might be mentioned that laryngeal neurosis, which may be evidenced by hoarseness as well as aphonia, is a definite clinical entity. Numerous instances of it were observed during the war, and Greene, in a discussion of Orton's<sup>2</sup> communication, recalled that in France and England during the 1938 Munich crisis, the almost epidemic hoarseness observed in many patients came to be known as "Munich sore throat" and was proved to be on a non-organic basis.

Not a great deal need be said about acute laryngeal conditions. Fever, malaise, rapid pulse, exanthemata, an elevated blood count and other systemic manifestations provide clues which are difficult to overlook. The warning is perhaps wise that diphtheria is always a possible diagnosis until it is adequately excluded; the disease still occurs and hoarseness is sometimes a first symptom.

This leaves us, then, with three conditions of extreme importance as the underlying causes of hoarseness, namely, tuberculosis, syphilis, and neoplasms, chiefly of the malignant variety. Whether or not tuberculosis is ever primary in the larynx is not a matter of great importance. The important consideration is that it is usually associated with pulmonary tuberculosis, that it is sometimes the first manifestation of an obscure and unsuspected thoracic disease, and that involvement of the larynx materially increases the risk of the pulmonary disease. In my personal experience laryngeal tuberculosis has invariably been associated with pulmonary tuberculosis.

The latter disease must therefore always be excluded in all cases of hoarseness, while laryngeal involvement must always be sought for in all cases of the pulmonary disease.

Hoarseness may be the first symptom to call attention to the presence of systemic syphilis. More often it is part of the general picture. Chancre is most unusual, but secondary and tertiary manifestations are not infrequent. The recurrent laryngeal nerve may be affected as part of the local process, as part of syphilis of the central nervous system, or as the result of pressure by an aneurysm or by a gumma of the mediastinum.

Benign neoplasms of the larynx are frequently responsible for persistent hoarseness. Papillomas are the most common variety, especially in children, but fibromas, myomas, lipomas, chondromas and cysts, especially of the epiglottis, may also occur. They are usually evident on proper examination. Papillomas may show a tendency to recurrence, even after adequate removal, until the young patients in whom they are most often seen outgrow them.

Malignant tumors of the larynx, as has already been intimated, are the most serious of the underlying causes of hoarseness, though, if they are recognized promptly, there is no cause for pessimism. The thing to be borne in mind about them, as well as about tuberculosis and syphilis, is that differential diagnosis is of vital importance, vital being used in its elementary significance—pertaining to life. The treatment of all three diseases is essentially different. The patient's life may be put in jeopardy if tuberculosis or syphilis is not recognized and if proper treatment is not promptly applied. His death warrant is signed if there is delay in the recognition of carcinoma. With the other two diseases it may be possible to recover lost ground. With malignancy it is never possible.

#### DIAGNOSTIC MEASURES

A discussion of diagnosis in a patient whose presenting symptom is hoarseness could well begin with the statement that the physician who makes such a diagnosis as

chronic laryngitis or laryngeal neurosis takes upon himself a heavy responsibility unless he has excluded every other possible cause of alteration in the voice. There is one peculiarly fortunate consideration about hoarseness. It points directly toward the structure, the larynx, which gives rise to the symptom. That consideration, on the other hand, may be disastrous rather than fortunate if the physician shuts his mind as to what it may imply and, in particular, if he fails to remember that even though the symptom arises in the larynx, the disease which causes it may lie at a considerable distance from that organ. The physician who fails to bear that fact in mind is the physician who treats a patient for hoarseness without proper investigation and who compounds the error by using local measures.

It is a safe rule that any hoarseness which has lasted more than two weeks demands investigation, which means considerably more than looking into the throat. An adequate study should include.

1. A complete history, including an inquiry into the patient's habits, use of tobacco and alcohol, occupation, and occupational environment, with particular respect to dust, smoke and gases.

2. A complete physical examination.

3. Indirect laryngoscopy.

4. Laboratory studies, including urinalysis, blood studies, blood serology, metabolic tests, and roentgenologic examination of the chest and sinuses.

5. Direct laryngoscopy, bronchoscopy or esophagoscopy, according to the indications in the special case.

6. Biopsy.

Certain points in this diagnostic regimen need special comment. It should be emphasized that while very few practitioners who are not specialists in otolaryngology are able to make a satisfactory examination of the larynx by mirrors, there is no reason why every practitioner should not train himself to do so. It is not the responsibility of the physician who is not a specialist to make a differential diagnosis. It is definitely his responsibility to know the normal,

so that he can recognize deviations from it and can refer the patient to a qualified specialist for such additional examinations as may be necessary.

Another point to be emphasized in indirect laryngoscopy is that the examination is not satisfactory unless there is a full view of the entire larynx and anterior commissure. Jackson's<sup>3</sup> warning should be remembered, that death lurks behind an overhanging epiglottis. If the desired view is not possible for this or any other reason, the patient should at once be referred for direct laryngoscopy, which is a hospital procedure, not an office method. Indirect laryngoscopy, however, is satisfactory and adequate in a very large proportion of cases. With patience it can be carried out even on a child. Without patience it is difficult to carry out even on an adult.

Special examinations should not be unduly delayed, the patient himself is likely already to have delayed too long. Damitz and Dill,<sup>4</sup> in an interesting analysis of 300 consecutive cases of hoarseness at the Henry Ford Hospital, found that the duration of hoarseness before the patients were seen ranged from eight and a half weeks in chronic non-specific laryngitis, to two weeks in benign neoplasms. In malignancy the duration was nine and a half months.

Biopsy is the definitive step of differential diagnosis. Without it a conclusive diagnosis is not possible, and upon its outcome depends the form of therapy to be followed in the special case. The specimen is usually small and the safety of the patient demands that it be passed upon by a well qualified pathologist.

#### THERAPY

Not a great deal need be said about therapy in a presentation on hoarseness, and what is said here is chiefly in the way of warning. The fundamental point has already been made, that the symptom must not be treated. Instead, the disease is treated when the etiology of the symptom has been established.

The first principle of treatment, regardless of the underlying disease, is absolute prohibition of the use of the voice. The



common advice to the patient to whisper if there is something important to be said is incorrect. A whisper causes more trauma to the larynx than does the full speaking voice. Almost the only exception to the rule that the voice should be completely rested is in laryngeal neurosis, in which rest only makes a bad matter worse.

General hygienic measures are important. If the patient works in an unfavorable environment, he should, preferably, change his occupation. Failing that, he should spend as much time as possible in the fresh air. Tobacco and alcohol are not permitted.

Local applications are seldom of value. Steam inhalations are useful in acute conditions, though moisture, rather than heat or any special drug, is responsible for whatever effects may be achieved. Expectorant mixtures are useful in conditions in which they are indicated. Opiates and their derivatives, which destroy the cough reflex—an overlooked form of therapy—should be avoided; they are extremely dangerous. Atropine, which dries up secretions, is also contraindicated. All measures of this kind sacrifice the ultimate good for temporary comfort.

When the basic cause of hoarseness is some systemic condition, treatment is the business of the appropriate specialist, who is not the otolaryngologist. It is particularly important in tuberculosis that management be in the hands of an experienced phthisiologist. Syphilis also demands expert care. If diphtheria is suspected as a possible cause of hoarseness, antitoxin should be given at once, in full doses. Laboratory confirmation is necessary for a final diagnosis, but delay in therapy may be fatal.

Hoarseness due to neoplasms, or, to state it more correctly, neoplasms of the larynx which give rise to hoarseness, are treated by local incision if they are benign, by laryngofissure, laryngectomy, or, in the occasional carefully selected case, by irradiation, if they are malignant. In late cases the only procedure is palliative, and it may fairly be said that every case in which tracheotomy is employed is one more illus-

tration of the danger of delaying a complete investigation of hoarseness.

#### SUMMARY AND CONCLUSIONS

1. Hoarseness is a symptom, the presence of which, for longer than two weeks, demands a thorough investigation. It may arise from a variety of causes, of which tuberculosis, syphilis and carcinoma of the larynx are the most important.

2. The business of the physician who is confronted with a patient complaining of hoarseness is not to treat the symptom but to diagnose the disease which gives rise to it.

3. The routine of investigation is described, and it is emphasized that biopsy should not be omitted in any case in which the diagnosis is not absolutely clear without it.

4. The general practitioner carries a heavy responsibility in the diagnosis of the causes of hoarseness, since he so often sees the patient first. He can readily train himself to perform indirect laryngoscopy. His function is not to make a differential diagnosis, but to recognize deviations from the normal, so that the patient can be referred to a specialist for appropriate further study.

5. Education of the lay public as to the possible implications of hoarseness is an essential phase of all cancer educational campaigns.

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#### DISCUSSION

*Dr. W. A. Wagner (New Orleans):* Dr. Taquino has brought forth something that is timely. I think that all of us laryngologists have seen malignancies late and when I say late perhaps I should emphasize that *too late*. I saw a malignancy recently—a patient who had been under treatment for better than six months by his family physician. Now he presents an inoperable malignancy of the larynx. If it were not for the fact that he developed the

mass in the upper clavicular region that did not precede but followed masses up along the upper cervical line of lymph node, he perhaps would not have been in to see me, but because of the mass which occurred the doctor thought there was some cause in the throat. There is no reason for that. I think that the general practitioner should be cautioned just as Dr. Taquino has done, that the early sign of malignancy of the larynx is hoarseness and when you wait for masses or other signs and symptoms you are going to have types of lesions that we, who are able to handle them properly, must resort to palliation. Palliation is all right and has been all right perhaps years ago, but today nobody should ask for palliation of a malignancy of the larynx when we are able today properly to handle malignancies of the larynx. It is true, as Dr. Taquino well brought the point out, that hoarseness is not the only sign of malignancy nor is hoarseness always indicative of malignancy. We see many lesions that are producing hoarseness that are non-malignant but unless the doctor—and I say the doctor, the general practitioner, is conscious of the variety of causes of hoarseness then only will we be able to get these patients early. If he is not we will not be able to save them; even though radiology has contributed much in the treatment of malignancy it has fallen short and when I say fallen short I mean that. We can read all the wonderful results by such men as Cutler and others who have had a tremendous experience with x-ray therapy but if we are going to resort to x-ray therapy to save all malignancies of the larynx we are going to fall short just like the radiologist with his x-ray apparatus. Irradiation does have merit, but early malignancy—and I feel sure of this when I speak these words—because I am merely quoting authorities—that those early malignancies are bet-

ter treated by surgical intervention than by irradiation.

Dr. Taquino should be complimented and this thought should be conveyed to the general practitioner not just this time but time and time again.

*Dr. Joseph Stamm* (New Orleans): I would like to ask one question. Would Dr. Taquino briefly tell us how he would handle leukoplakia?

*Dr. Taquino* (in closing): I would like to emphasize one point. Surgery can not be replaced by x-ray therapy. Surgery is the ideal thing to do when dealing with a malignant growth. I think results from operation are so far superior that one ought not to consider other therapy except in cases where it is a physical impossibility to do an operation. I have a patient on whom I have just done a tracheotomy five days ago. The man walked in the office. He had refused to see doctors. He has definitely got a carcinoma of the larynx. I did a tracheotomy on him—he has mediastinal involvement, so there was nothing to do but palliative treatment. How much good it will be I do not know. He will probably get along just as well with tracheotomy as with x-ray therapy.

In school, I teach all of my students to become familiar with the use of the laryngeal mirror, thus being able to recognize a normal larynx from an abnormal one. The student should be able to differentiate between a normal and abnormal condition, so when the abnormal one presents itself he should be able to recognize it immediately and see that the patient is placed in the proper hands.

I also tell them when an abnormality appears to ask themselves the question,—Am I dealing with a cancer, and then prove whether or not it is present and be sure also that you prove the diagnosis before advising the patient that he has or has not a cancer; do not make any rash statements or use rash judgment in the treatment of the patient.



## NEW ORLEANS

## Medical and Surgical Journal

*Established 1844*

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SOUTHERN REGIONAL  
CONFERENCE

The Council on Medical Service of the A.M.A. is sponsoring a Southern Regional

Conference to be held at the Roosevelt Hotel in New Orleans Thursday and Friday, October 23-24. This conference will include representatives from the States of Texas, Oklahoma, Arkansas, Mississippi, Alabama and Louisiana. The purpose of the meeting is to discuss certain problems of these various states: Liaison Between the A.M.A. and the Component Medical Societies; The Washington Legislative Picture; Medical Society Public Relations; Prepayment Medical and Surgical Care Plan Problems; Industrial Health Problems of the South; and Rural Health Problems.

The President-elect of the A.M.A., Dr. R. L. Sensenich has tentatively agreed to address the meeting and addresses of welcome will be made by Dr. Gilbert C. Anderson, President of the Louisiana State Medical Society and Dr. H. Ashton Thomas, President of the Orleans Parish Medical Society.

The meeting is being held under the chairmanship of Dr. James R. McVay of the national organization and Dr. A. V. Friedrichs of the State Society. The Louisiana State University Medical School and the Tulane University School of Medicine have been invited to send representatives to this conference. All physicians who may be interested in these problems are also invited to attend.

A full program may be found on pages 134, 135 of this issue of the Journal.

## KALA-AZAR IN LOUISIANA

The recent report by H. D. Ecker and J. M. Lubitz of two cases of visceral leishmaniasis in Louisiana should sharpen the suspicions of physicians concerning the possibility of kala-azar in patients complaining of symptoms or signs consistent with this disorder. This is particularly true now because of the increase in amount and rapidity of world travel and especially because of the return of great numbers of veterans from endemic areas. In view of the fact that the incubation period may exceed one year, infected individuals may be discharged from the Services in apparently good physical condition. Obviously such

possibility will exist months after the withdrawal of the last of our armed forces.

The diagnosis may be suspected in patients with fever, weight loss, anemia, leukopenia, abnormal proteins and enlarged liver and spleen. Confirmation depends on the identification of the Leishman-Donovan bodies by means of culture, blood or tissue examination. It is recommended that repeated sternal marrow studies be done before resorting to the more hazardous liver and splenic punctures for the parasite occurs in groups or colonies and one or more marrow smears may yield negative results even in the hands of experienced examiners.

Treatment with pentavalent antimony compounds or stilbamidine is highly effective. Stilbamidine offers hope of cure in those instances which fail to respond to the pentavalent antimonials. Toxicity with any of these drugs is low when proper precautions of administration are observed.

Drs. Ecker and Lubitz are to be commended on their clinical acumen in recognizing and successfully treating the first two cases of kala-azar in Louisiana.

## THE DIAGNOSIS OF MALARIA

Inquiry made at the Louisiana State Charity Hospital in New Orleans has revealed that no cases of malaria endemic to Louisiana have been treated in the past three years. Further, patients sent in to Charity Hospital with a diagnosis of malaria have proved to be suffering from other febrile disorders in very many instances. Thus, most of the malaria present in our state is treated by country practitioners. These busy men will welcome the improvements made in the technic of staining plasmodia. Thick films are not made as thick as formerly. The amount of blood, 2 to 4 small drops, is spread, not stirred, with a clean wooden applicator, match or glass rod, so that when the slide is turned vertically the blood does not immediately form a definite drop at the dependent point; instead of flowing quickly it should appear to crawl. The slide is then placed flat and allowed to dry. Each slide should bear

some identification mark. Walker's method of staining with Giemsa Blue which demonstrates the malarial parasites most beautifully is as follows:

Dip for one second in methylene blue-phosphate solution.<sup>1</sup>

Wash gently in distilled water to remove excess blue solution.

Place *face downward* on a curved staining plate in diluted Giemsa stain<sup>2</sup> for eight to ten minutes (1 drop to each cubic centimeter of buffer water<sup>3</sup>).

Drain and dry thoroughly with gentle heat.

Examine under oil immersion. The *margin* of the thick film *usually shows better color differentiation than does the center*.

Note the absence of red blood cells, the rich blue-violet color of the nuclei of leukocytes, the red-violet dark cytoplasmic granules of polymorphonuclears, the coppery-red eosinophilic granules, groups of pale violet platelets. The morphology of leukocytes is well preserved. Each parasite consists of one or more masses of reddish chromatin closely associated with a variable amount of greenish blue cytoplasm. Pigment may be recognized in the larger parasites. Parasites are easily distinguished from ruptured leukocytes, platelets, bacteria, spores and other artefacts. Many bacteria are present in blood from punctures of skin and are ignored.

Physicians interested may obtain these solutions at a very nominal cost from Dr. A. J. Walker of the Department of Tropical Medicine at Tulane University School of Medicine.

### 1. Methylene blue-phosphate

Methylene blue	0.5 Gm.
Disodium monohydrogen phosphate, anhydrous ( $\text{Na}_2\text{HPO}_4$ )	1.5 Gm.
Monopotassium dihydrogen phosphate ( $\text{KH}_2\text{PO}_4$ )	0.5 Gm.
Distilled water	400 cc.

Filter before use; avoid evaporation.

### 2. Giemsa Stain: any well known brand (certified) in liquid form or:—Giesma powdered stain (certified)

0.75 Gm.	
Pure methyl alcohol	65 cc.



Pure glycerine ..... 35 cc.  
 Shake well in bottle with glass beads and  
*keep tightly stoppered at all times.*  
 Use from 30 cc. or 60 cc. bottles.

3. *Buffer Water*

Disodium monohydrogen phos-

phate anhydrous ..... 7 parts  
 Monopotassium dihydrogen phos-  
 phate ..... 4 parts  
 Mix thoroughly in a mortar. Add 2.0 Gm.  
 to 1000 cc. distilled water. Renew if  
 slightly cloudy.

## ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

*An informed profession should be a wise one.*

### VETERANS ADMINISTRATION AGREEMENT FOR MEDICAL CARE OF VETERANS

In December, 1946 the Louisiana State Medical Society entered into an agreement with the Veterans Administration for medical care of veterans with service connected disabilities. The object of this agreement was to furnish for veterans medical care by the physicians in their home town and obviate the necessity of going to another locality for service.

During the past months since the contract has been in effect there have been some complaints concerning the operation of this agreement. In order that an appropriate investigation may be made concerning inadequacies of the plan it is requested that comment be furnished by members of the State Society concerning their experience with this project. In submitting such information it is desired that full facts in connection with specific cases be given. The data will be compiled and an effort will be made to have all discrepancies clarified.

Further information will be carried in future issues of the Journal.

### SOUTHERN REGIONAL CONFERENCE OF AMA TO BE HELD IN NEW ORLEANS IN OCTOBER

The Southern Regional Conference sponsored by the Council on Medical Service of the American Medical Association will be held in New Orleans at the Roosevelt Hotel on Thursday, October 23, and Friday, October 24. Arrangements for the confer-

ence are being handled by the Council on Medical Service and Public Relations of the Louisiana State Medical Society. Dr. A. V. Friedrichs is chairman of the arrangements.

The States of Alabama, Mississippi, Texas, Oklahoma, Arkansas, Tennessee, and Louisiana will participate in the conference. Committees invited to attend the conference from the mentioned State Societies are: Public Relations Committee, Prepayment Medical and Surgical Care Plan Committee, Industrial Health Committee, Rural Health Committee and officers and directors of the various state and county (parish) medical societies in the South.

While the conference is primarily a meeting of the officers, directors, and committees of the various State Societies in the South, any doctor interested in the meeting is invited to attend. The meeting is open to all physicians, particularly those interested in the expansion of medical care in industrial and rural areas.

Numerous distinguished guests from the American Medical Association are scheduled to appear on the program together with many well known representatives from the various states.

The meeting will be opened by Addresses of Welcome by Dr. Gilbert C. Anderson, President, Louisiana State Medical Society, and Dr. H. Ashton Thomas, President of the Orleans Parish Medical Society. American Medical Association representatives scheduled to appear on the program on Thursday, October 23, are Dr. James R.

McVay, Chairman of the Council on Medical Service of the AMA, Dr. George F. Lull, Secretary and General Manager of the AMA, and Dr. Joseph S. Lawrence, Director of the Washington Office of the Council on Medical Service of the AMA.

The subject "What is Good Medical Society Public Relations" will be discussed on Thursday morning with Henry S. Johnson, Director of Public Relations of the Medical Society of Virginia, as Moderator.

The afternoon session of the Thursday program has been devoted to a discussion of "Prepayment Medical and Surgical Care Plan Problems".

The program on Friday morning, October 24, will be devoted to "Industrial Health Problems of the South", with Dr. Stanley J. Seeger, Chairman of the Council on Industrial Health of the AMA, as Moderator.

"Rural Health Problems" will be the topic for discussion on Friday afternoon. Dr. J. Paul Jones of Camden, Alabama, of the Committee on Rural Medical Service of the AMA, will be the Moderator at this session.

Each morning and afternoon session will have panel discussants to lead the discussion of the problems and everyone in attendance may participate actively in the discussions.

A cocktail party has been scheduled for Thursday evening, 5 to 7 p. m. in the Roosevelt Hotel. The party is scheduled with the object of offering an opportunity to members of the State Society to meet the visiting guests from the AMA and other State Societies.

Following is a copy of the tentative program as announced by the Council on Medical Service of the AMA.

#### A TENTATIVE PROGRAM

For

#### THE SOUTHERN REGIONAL CONFERENCE

Roosevelt Hotel, October 23-24

New Orleans, La.

Chairman—James R. McVay, M. D., Chairman  
Council on Medical Service

American Medical Association

THURSDAY, OCTOBER 23

9:00 a. m.—Registration

9:30 a. m.—Address of Welcome

Gilbert C. Anderson, M. D., President, Louisiana State Medical Society

H. Ashton Thomas, M. D., President, Orleans Parish Medical Society

9:45 a. m.—Purpose of Meeting

James R. McVay, M. D.

10:00 a. m.—Liaison between AMA and the Component Medical Societies, George F. Lull, M. D., Secretary and General Manager, AMA

10:30 a. m.—The Washington Legislative Picture  
Joseph S. Lawrence, M. D., Director, Washington Office of the Council on Medical Service of the AMA  
*What is Good Medical Society Public Relations?*

11:00 a. m.—Public Relations Round Table Discussion

*Moderator*—Henry S. Johnson, Director of Public Relations, Medical Society of Virginia

*Panel Discussants*—

A. V. Friedrichs, M. D., Chairman, Council on Medical Service and Public Relations, Louisiana State Medical Society

Donovan C. Browne, M. D., Chairman, Public Relations Committee, Orleans Parish Medical Society

Richard Graham, Executive Secretary, Oklahoma State Medical Association

W. R. Brooksher, M. D., Secretary, Arkansas Medical Society

Holman Taylor, M. D., Secretary, State Medical Association of Texas

1:00 p. m.—Luncheon (Dutch)

#### THURSDAY, OCTOBER 23

Afternoon Session

2:30 p. m.—*Prepayment Medical and Surgical Care Plan Problems*

Prepayment Medical and Surgical Care Plan Round Table Discussion  
*Moderator*—Charles R. Henry, M. D., Chairman Committee on Medical Service and Public Relations, Arkansas Medical Society, Little Rock, Arkansas

*Panel Discussants*—

O. B. Owens, M. D., President, Louisiana Physicians Service, Alexandria, Louisiana

W. R. McBee, Executive Director, Group Medical and Surgical Service, Dallas, Texas



Ed S. Moore, Manager, Hospital Service Corporation of Alabama, Birmingham, Alabama

Edward F. Groner, Manager, Hospital Service Association of New Orleans, New Orleans, Louisiana

Report of States—

Alabama—Mississippi—Texas—

Oklahoma—Arkansas—Tennessee—Louisiana

FRIDAY, OCTOBER 24

Morning Session

10:00 a. m.—*Industrial Health Problems of the South*

Industrial Health Round Table Discussion\*

*Moderator*—Stanley J. Seeger, M. D., Chairman, Council on Industrial Health of the AMA

*Panel Discussants*—

Lloyd Noland, M. D., Medical Director, Tennessee Coal, Iron and R. R. Co., Fairfield, Alabama

J. T. Scott, Jr., M. D., Chairman, Committee on Industrial Health, Louisiana State Medical Society, New Orleans, Louisiana.

Carl Nau, M. D., Prof. of Physiology, Preventive Medicine and Public Health, University of Texas Medical School, Galveston

Jean Felton, M. D., Superintendent, Health Dept., Monsanto Chemical Company, Clinton Laboratories, P. O. Box 1991, Knoxville, Tenn.

O. M. Derryberry, M. D., Chief of Employee Health Services Division, Tennessee Valley Authority, Chattanooga, Tennessee

\*The Industrial Health group will meet separately on Friday afternoon to discuss the technical problems of industrial programs.

12:15 p. m.—Luncheon (Dutch)

FRIDAY, OCTOBER 24

Afternoon Session

2:00 p. m.—*Rural Health Problems*

Rural Health Round Table Discussion  
*Moderator*—J. Paul Jones, Camden, Alabama, Committee on Rural Medical Service, AMA

*Panel Discussants*—

Allen T. Stewart, M. D., Member National Committee on Rural Medical Service, Lubbock, Texas

Guy R. Jones, M. D., Chairman, State Society Committee on Rural Medical Service, Lockport, La.

Chairman, Mississippi Rural Health Committee

A. S. Buchanan, M. D., Prescott, Arkansas State Society Committee on Rural Medical Service

The preceding program is a tentative program and invitations have been extended to personnel listed thereon. However, final acceptance of their appearance on the program was not received when this article went to press.

## TRANSACTIONS OF ORLEANS PARISH MEDICAL SOCIETY

Sept. 9. Orleans Parish Radiological Society, 7:30 p. m.

Sept. 15. Hotel Dieu Staff, 8 p. m.

Sept. 18. Clinico-pathologic Conference, Touro Infirmary, 12 noon.

Veterans Administration Hospital Staff, 8 p. m.

Sept. 19. Lakeshore Hospital Staff, 8 p. m.

Sept. 24. French Hospital Staff, 8 p. m.

Sept. 25. DePaul Sanitarium Staff, 8 p. m.

Sept. 26. New Orleans Dispensary for Women and Children Staff, 8 p. m.

Oct. 1. Mercy Hospital Staff, 8 p. m.

Oct. 2. Clinico-pathologic Conference, Touro Infirmary, 12 noon.

Executive Committee, Baptist Hospital, 8 p. m.

Oct. 3. Ochsner Clinic Staff, 8 p. m.

Oct. 6. Board of Directors, Orleans Parish Medical Society, 8 p. m.

Oct. 7. Eye, Ear, Nose and Throat Staff, 8 p. m.

Oct. 8. Woman's Auxiliary, Orleans Club, 3 p. m.

Touro Infirmary Staff, 8 p. m.

### NEWS ITEMS

Dr. Earl Conway Smith was elected president of the New Orleans Gynecological and Obstetrical Society at the annual meeting of this organization July 1. Other officers elected were: Dr. W. D. Beacham, president-elect; Dr. Curtis H. Tyrone, vice-president; Dr. John S. Herring, secretary; and Dr. Harry Meyer, treasurer.

Dr. G. J. von Langermann was recently elected recording secretary of the Altrusa Club of New Orleans.

Drs. W. D. Beacham, John W. Weed and B. Bernard Weinstein attended the meeting of the American Society for the study of Sterility in Atlantic City.

Dr. Weinstein presented a paper before the Society on the "Surgical Management of the Tubal Factor in Sterility", and presided over a meeting

of the Research Correlating Committee of which he is chairman.

N. J. TESSITORE, Secy.

## LOUISIANA STATE MEDICAL SOCIETY NEWS

### C A L E N D A R

#### PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

#### 1948 ANNUAL MEETING

Following is personnel of Advisory Committee and list of chairmen of committees who have been appointed to handle the forthcoming meeting of the State Society in Monroe, April 12-14, 1948.

Advisory Committee: John G. Snelling, Chairman, A. Scott Hamilton, Co-Chairman, C. P. Gray, Sr., James Q. Graves, George Wright and DeWitt T. Milam.

Badges, Signs and Decorations: Dr. Wood Scott.

Banquet: Dr. C. P. Gray, Jr.

Budget and Finance: Dr. Henson Coon.

Commercial Exhibits: Dr. Clifford Johnson.

Entertainment: Dr. C. B. Flinn.

Golf: Dr. Fred Marx.

Hotel and Meeting Rooms: Dr. J. W. Cummins.

Lanterns and Sound Equipment: Dr. M. W. Hunter.

Luncheons: Dr. Henry Guerriero.

Program: Dr. Glenn Gallaspy.

Publicity: Dr. W. L. Bendel.

Registration: Dr. P. L. Perot.

Scientific Exhibits: Dr. J. E. Walsworth.

Transportation: Dr. George Varino.

#### JARRETT RESIGNS

Dr. Lewis E. Jarrett who has been director of Touro Infirmary since April 7, 1944 has resigned his position at this institution. Dr. Jarrett came to New Orleans from Richmond, Virginia. In his short stay in this city he has become very well liked and very popular. Last year he was elected president of the Louisiana Hospital Association. It is with considerable regret that the medical profession will see Dr. Jarrett leave the city.

#### NEW SCHOOL OF PREVENTIVE AND TROPICAL MEDICINE

Dr. Rufus C. Harris, president of the Tulane University has announced that the medical school is prepared to give a new course in the Department

of Tropical Medicine and Public Health which will lead to a master's degree in public health (tropical medicine). All of the required courses that will lead to a master's degree in public health will be given, plus extra courses in tropical medicine. Preventive medicine and public health activities will be those that are given at the important schools of public health throughout the country but an addition of the electives in tropical medicine for certain required courses will qualify the man who wishes to practice in the tropics to be a well rounded public health officer as well as skilled in the field of tropical medicine.

#### AMERICAN HOSPITAL ASSOCIATION

The forty-ninth annual convention of the American Hospital Association will be held Monday, September 22-25, in St. Louis, Missouri. There will be an opening general session on the first day, following which the convention will be broken into four sections on Professional Practice, Administrative Practice, Hospital Planning and Plant Operation and Special Aspects of Hospital Administration. The final afternoon session will consist of a resumé of the discussion in all of the special sessions under the topic "American Hospitals Today".

#### AMERICAN ACADEMY OF GENERAL PRACTICE OF NEW ORLEANS

At an organization meeting of the American Academy of General Practice of New Orleans held on August 20, Dr. Joseph C. Menendez was elected president, Dr. F. A. Fatter, vice-president and Dr. R. E. Gallaspy, secretary-treasurer. Named to serve as members of the Board of Directors are Dr. E. L. Leckert, Dr. W. A. Gallaspy, Dr. Charles Moseley, Dr. Lucien C. Delery, Dr. Joseph J. Ciolino, Dr. Theo F. Kirn, Dr. N. J. Chetta, Dr. George Barnes and Dr. Frank Gallo. Dr. J. P. Sanders, of Shreveport, president of the American Academy of



General Practice of Louisiana and a representative on the Board of Directors of the national organization, addressed the group.

#### CONSTRUCTION OF V. A. HOSPITALS TO BE DELAYED

On account of the increasing cost of building of hospitals the V. A. hospital project necessarily will have to be considerably delayed. Large amounts of money have been voted for these hospitals but the cost has gone up so rapidly that the almost one billion dollars that is available will not begin to complete the program as outlined by General Bradley and Colonel Hardin.

The V. A. hospital which is to be built back of the Charity Hospital in New Orleans has already been started to a limited degree. The gas plant has been removed from the property, the ground has been cleared and the preliminary test piling has been initiated.

This delay is unfortunate as there is a very distinct need and want for the new institutions. It might be added that hospital costs have increased from 85 cents a cubic foot in 1945 to \$1.25 in 1946, to \$1.80 as of today.

#### POSTGRADUATE COURSES—AMERICAN COLLEGE OF PHYSICIANS

The American College of Physicians announces a series of courses in various phases of internal medicine. These courses are given in various portions of the country and are scheduled to run from September 1 until the middle of December. The detailed programs for the first five have been issued. The first is internal medicine at the University of Pittsburgh Medical Center and other Pittsburgh institutions from September 1-13. Course No. 2 is on psychosomatic medicine under the direction of Dr. F. G. Ebaugh and will be given at the University of Colorado Medical Center from September 8-20. Course No. 3, is on the mechanics of disease under the direction of Dr. George W. Thorn of Peter Bent Brigham Hospital where the course will be held for two weeks beginning September 15. Course No. 4 will be of a week's duration under the direction of Dr. W. B. Castle at various Boston institutions. The course will be devoted to subjects on hematology and blood disorders and will start October 13. Course No. 5 is likewise for one week and will be held under the auspices of the University of Pennsylvania Graduate School of Medicine with Dr. J. H. Comroe, Jr. acting as director. This course will be on the physiological basis for internal medicine and is scheduled to begin October 20.

Subsequent courses will be conducted at the Southwestern Medical College, Dallas, Texas, on cardiovascular disease; chemotherapy at the Boston University School of Medicine; internal medicine at the University of Wisconsin Medical School, Madison; at the Massachusetts General Hospital on

recent advances in the diagnosis and treatment of cardiovascular disease; gastroenterology at the Graduate Hospital of the University of Pennsylvania; cardiology at the Yale University School of Medicine, and the last one that has been provided for is one in general medicine at the University of Texas School of Medicine.

These courses are open primarily to the Fellows and Associates of the American College of Physicians. In the event that within a period of three weeks before a course commences the minimal registration figures have not obtained, non-members may take the course. Minimal registration, depending on the institution and the course, is from 25 to 70. The fees vary from \$60-\$120 for members of the College and for non-members double the figures. Further information may be obtained from Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Pa.

#### LOUISIANA STATE SOCIETY OF MEDICAL TECHNOLOGISTS

The Louisiana State Society of Medical Technologists, in cooperation with the American Society of Medical Technologists will sponsor a four day seminar at Loyola University in New Orleans September 29-October 2, 1947. Registered medical technologists from Texas, Florida, Arkansas, Mississippi and Louisiana have been invited to attend and all interested doctors and students are invited to be guests. The program will consist of lectures and demonstrations on mycology and hematology to be given by outstanding medical men of New Orleans. Anyone planning to attend this seminar should notify Miss Dorothy Dickinson, Secretary of the Louisiana State Society of Medical Technologists, P. O. Box 1368, Alexandria.

#### MEETING MISSISSIPPI VALLEY MEDICAL SOCIETY

The 12th Annual Meeting of the Mississippi Valley Medical Society at Burlington, Iowa, Oct. 1-3, will have over 30 clinician-teacher speakers. Oct. 1 will feature an all-St. Louis program conducted by clinical teachers from St. Louis and Washington Universities. On Oct. 2 there will be speakers from various medical centers including Dr. E. L. Bortz, President, American Medical Ass'n., Dr. I. H. Neece, President, Illinois State Medical Society, Dr. M. B. Simpson, President, Missouri State Medical Assn., and Dr. H. A. Spilman, President, Iowa State Medical Society. There will be a social hour and banquet on this date. The afternoon program will be devoted to presentations by a group from the University of Iowa. Oct. 3 will feature an all-Chicago program with a number of well-known clinical teachers from Chicago medical schools. A Clinico-Pathologic Conference and a Round Table luncheon will be featured on this date.

### THE EYE-BANK FOR SIGHT RESTORATION, INC.

An affiliated "Eye-Bank" has been organized in New Orleans, La., which will have the cooperation of the Louisiana State University Medical School and the Tulane University Medical School, it was announced here at national headquarters of The Eye-Bank for Sight Restoration, Inc. Other affiliated Eye-Banks are functioning in Boston and Chicago.

The new Eye-Bank is located in the Hutchinson Memorial Building, New Orleans, and Mrs. Orville Ewing is serving as Executive Director. The officers are Charles E. Fenner, President; Dr. William B. Clark, 1st Vice President; Dr. George L. Hardin, 2d Vice President; John F. Reilly, Treasurer; and John W. Sims, Secretary.

### ACADEMY-INTERNATIONAL OF MEDICINE

This organization announces that as a service to the profession it is offering to mail, upon request, to any member of the Louisiana State Medical Society a complimentary copy of their medical and surgical film catalogue which contains a list of the films that are now available and the source from which they may be obtained by the borrower.

Requests for the catalogue should be sent to the Academy - International of Medicine, 214 West Sixth Street, Topeka, Kansas.

### MICROFILM SERVICE STILL AVAILABLE

Through the microfilm service of the Army Medical Library, physicians, libraries and professional workers almost anywhere in the world may obtain facsimile replicas of the great bulk of existing medical literature on 35 millimeter film, according to Colonel J. H. McNinch, Commandant of the Army Medical Library.

Any page of a medical journal, book or manuscript is photographed with high-speed cameras in the microfilm process. The physician or researcher requesting the material receives the film reproduction reduced to the size of a large postage stamp for each page. These pages can be read either in small-size film reviewers which enlarge the tiny microfilm, or they can be projected to large, readable size in special machines now available in many libraries and research centers. A whole book on microfilm takes only as much space as the corner of a coat pocket.

Costs are moderate for the microfilm duplicating service that brings the world's medical literature into the office of any physician however remote. Articles in medical periodicals are duplicated on microfilm for fifty cents each. Books are duplicated for fifty cents for each fifty pages or fraction thereof. Photostats are priced at fifty cents for each ten pages or fraction thereof for any single volume. There are certain restrictions on photoduplication to protect the rights of copyright owners.

### INDUSTRIAL HYGIENE DIVISION— FEDERAL SECURITY AGENCY

Formation of an Atomic Radiations Unit in the Chemical Section of the Industrial Hygiene Division, U. S. Public Health Service, was announced by Dr. J. G. Townsend, Chief of the Division. Duncan Holaday, Engineer (R), is in charge of the new Unit.

The new Unit will advise and assist State industrial hygiene units in detecting and evaluating health hazards produced by the use of radio-active isotopes and high energy machines such as x-ray machines and betatrons.

### PHYSICIAN WANTED

The town of Vinton, Louisiana is in need of a physician. Population approximately 3,000. At present the nearest doctors are 15 miles east and 12 miles west of town. Equipment for sale by retiring physician. Contact Mrs. Jo McGann, Clerk, Town of Vinton.

### HEALTH OF NEW ORLEANS

The Bureau of the Census, Department of Commerce, from the figures reported by the New Orleans Health Department announces that for the week ending July 5 there were 84 deaths in the City of New Orleans, 50 being in the white population and 34 in the nonwhite. Of these deaths six were in infants under one year of age; four white and two colored. The week which terminated July 12 showed an increase of 70 deaths; the unusual number of 106 occurring in the white population and 48 in the colored. An increase was also noted in the number of infant deaths, there being a total of 16 with ten of these occurring in the white race. There was a decrease of 40 deaths in the city during the week which ended July 19. Seventy-two white citizens and 42 colored expired this week. The number of infant deaths was the same as for the preceding week, however the majority of these occurred in the colored population; 11 colored and five white. The report for July 26 indicated 152 deaths which was considerably higher than the number for the week of July 19 and exceeded the three year median corresponding week by 21. This week the deaths were divided 86 and 66 between the white and colored respectively. The week of August 2 showed a drop in number of deaths over the previous week this year, however the number was over the three year median. There were 137 deaths reported; 92 white, 45 colored and 17 in children under one year of age.

### INFECTIOUS DISEASE IN LOUISIANA

The weekly morbidity report for the State of Louisiana for the week ending July 5 showed pulmonary tuberculosis leading all other reported diseases. There were 45 cases of pulmonary tuberculosis listed followed by 25 of measles, and 14 of bacillary dysentery. No other diseases were re-



ported in numbers greater than ten. There were, however, four cases of poliomyelitis reported in Caddo Parish and two cases of meningococcus meningitis reported; one each from Pointe Coupee and Richland Parishes. Cancer led all reportable diseases for the week ending July 12 when there were 44 cases reported. Pulmonary tuberculosis followed with 34 cases and unclassified pneumonia with 22. Report of poliomyelitis cases decreased this week to one case from St. Landry Parish. Pulmonary tuberculosis and cancer still headed the lists of diseases reported for the week ending July 19. This week there were 39 of the former and 37 of the latter reported, and again, the only other disease reported in number greater than ten was unclassified pneumonia with 16 instances. One case of meningococcus meningitis was reported from St. Bernard Parish and one case of poliomyelitis from Caddo. The number of pulmonary tuberculosis cases decreased during the week ending July 26 to 12 cases, however cancer was still in the lead with 49 cases, followed by 33 of unclassified pneumonia, 15 of whooping cough and 12 of amebiasis. Poliomyelitis was still in evidence in Caddo Parish where two additional cases were reported and another was reported in Calcasieu. Caddo Parish also reported one case of meningococcus meningitis and Ouachita Parish reported two cases of this disease.

#### MONTHLY MORBIDITY FOR VENEREAL DISEASES STATE OF LOUISIANA

Month Ending June 30, 1947

	Total This Month	Total Previous Months	Total to Date 1947
Chancroid	49	280	328
Gonorrhea	1118	6279	7397
Granuloma Inguinale	23	82	105
Lymphopathia Venereum	3	38	41
Syphilis	860	4908	5768

#### FRANK BROSTROM

1894-1947

Dr. Frank Brostrom died suddenly in New Orleans on July 31. Dr. Brostrom was one of the well known group of orthopedic surgeons in New Orleans. He was connected with the staff of Touro Infirmary and the New Orleans Dispensary for Women and Children. He came to New Orleans some fifteen years ago, already well trained in his specialty. He had been with the Infantile Paralysis Foundation in Warm Springs, Georgia for a period of time and is said to have attended the late President Roosevelt. Dr. Brostrom was not only an outstanding man in his field but also was notable for the kind and splendid service he gave to his indigent patients.

Shortly after migrating to New Orleans Dr. Brostrom became a member of the State Medical Society. He was a graduate of Jefferson Medical College in Philadelphia.

## BOOK REVIEWS

*Occupational Diseases of the Skin:* By Louis Schwartz, M. D., Louis Tulpian, M. D. and Samuel Pack, B. S., M. D. 2d ed. rev. Philadelphia, Lea & Febiger, 1947. Pp. 964, Illus. pl. Price, \$12.50.

This is a thoroughly revised and improved text. It should be of especial interest to those practicing industrial medicine and surgery, employers in occupations presenting hazards to the employee, to the insurer and to those eligible or ineligible of employment. Compensation laws of the several states are described and an extensive bibliography are included.

Sensitivity to external irritants showing the influence of race, color, perspiration, diet, age, sex, season, cleanliness and either existing or previous dermatoses, are fully discussed.

Patch testing is outlined and its value after the development of a dermatitis venenata or its use before employment is stressed. Pages and pages of detailed descriptions of irritations, with their causes, methods of weeding out diseases or other causes and methods of approach are contained in

this volume, the life's work of Dr. Louis Schwartz in his office as Industrial Surgeon of the U. S. Public Health Service with the able assistance of Drs. Tulpian and Pack. It is a volume of experience detailed to keep the employer and employee out of the law court and a necessary text for the interested physician.

M. T. VAN STUDDIFORD, M. D.

*If You Need an Operation:* By Richard A. Leonardo, M. D., Ch. M., F.I.C.S. New York, Froben Press, 1947. Pp. 198. Price, \$3.00.

If one realizes the mental state that prospective surgical patients and their relatives go through, then the publication of this book fulfills a very necessary role—one might say it should be part of the preoperative treatment.

Confusing thoughts which naturally arise in the patient's mind are simply and lucidly classified.

The medical "language" used should not be beyond the grasp of the average patient (or their relatives mind you) and the author deals intelligently from the surgeon's and patient's points of

view, with the general outline of the object and procedure of the operation.

But, to certain types of patients, a little knowledge is a dangerous thing, and as the author deals with postoperative complications as well, such highly strung patients would do well not to read the book.

In general, however, it is felt that both patient and surgeon will greatly benefit from a perusal of this book.

DENIS ROSENBERG, M. D.

*Diseases of the Skin, for Practitioners and Students:* By George Clinton Andrews, A. B., M. D. 3d ed. Philadelphia, W. B. Saunders Co. 1946. Illus. Pp. 937. Price, \$10.00.

This edition, like its predecessors is ideal for the student and practitioner. Emphasis has been placed on removing much of the old and obsolete material which was "carried over" from older authorities and a concise, condensed description of new discoveries has filled the space. This edition has a greater amount of printed matter due to a better utilization of the space on each page.

The Chapter on Symptomatology and General Diagnosis makes for a better understanding of the material in orderly form. Roentgen ray therapy, which is excellently described and radium therapy are brought up to date. Dermatitis venenata is enlarged upon and the role of focal infection is stressed in all the toxic manifestations of dermatoses. The use and misuse of the sulfones and antibiotics are fully discussed. The author has spared no effort in getting outside assistance for such subjects as fungous diseases, pathology of varicosities and occupational diseases. This edition is highly recommended for the ready-reference shelf of the medical profession.

M. T. VAN STUDDIFORD, M. D.

*Muscle Testing, Techniques in Manual Examination:* By Lucille Daniels, M. A., Marian Williams, M. A. and Catherine Worthingham, M. A. Philadelphia, W. B. Saunders Co., 1946. Pp. 189, illus. Price, \$2.50.

This book presents a detailed yet simplified and coordinated approach towards manual muscle testing. It is a practical manual designed primarily for teaching the student to analyze and grade movement in terms of specific muscular action. The introduction briefly but adequately covers the origin and development of muscle testing in this country, and a helpful chart shows nine different methods of muscle testing which have been used by different individuals or groups.

The book deals with muscle groups of defined body areas, and emphasis has been placed on the testing of prime movers in relation to the principal joints of each segment of the body. The assimilation of valuable anatomic information concerning muscle insertions and origins, joint ranges, and

nerve distribution with physiological data concerning prime movers, fixation of specific group action and synergistic action, along with clearly illustrated methods for testing neuromuscular conditions in a systematized order meets a definite need for students, physical therapists, and physicians and surgeons interested in the teaching and practice of orthopedic surgery and physical medicine.

Another outstanding feature is the abundance of clear and concise diagrammatic drawings which amply supplement the text.

The only undesirable feature is the lack of a more permanent binding.

R. M. KIMBALL, M. D.

*Therapeutic Exercise:* By F. H. Ewerhardt, M. D. and Gertrude Riddle, B. S., R. N., R. P. T. Philadelphia, Lea & Febiger, 1947. Pp. 152. Price, \$2.50.

This book is concise manual designed for students of physical education, occupational therapy, and physical therapy. The material is presented in a didactic fashion with anatomic and physiologic consideration of joint movements and their analysis, particular emphasis having been placed on the musculature and nerve supply of the extremities.

The physiology and special application of therapeutic exercises are well presented with adequate space devoted to the indications and contraindications, as well as the specific exercises utilized in the treatment of weakness of the feet, abdomen, and the low back, and the preoperative management of scoliosis.

The section on the teaching of posture, and the application of exercises in cardiac and respiratory disease, as well as other common conditions, should be of benefit to the general practitioner.

The section on poliomyelitis is concerned primarily with the Kenny Method during the acute phase and the methods of muscle function testing and muscle re-education during the latter phases, without, however, any reference to the use of braces.

The section on spastic paralysis is well balanced, and presents the current methods available for rehabilitation of the various types of this disorder.

The text suffers by the lack of illustrations, and the didactic approach necessary for conciseness, but it is a handy reference book for surgeons and physiotherapists who wish to give the patient a precise program of exercise, and it adequately fulfills its object as a teaching manual.

R. M. KIMBALL, M. D.

#### PUBLICATIONS RECEIVED

American Medical Association, Chicago: Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association for 1946.

McGraw-Hill Book Company, New York: The Years After Fifty, by Wingate M. Johnson, M. D.



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### RADIOTHERAPY FOR GYNECOLOGIC CANCER\*

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AND

JOSEPH V. SCHLOSSER, M. D.†  
NEW ORLEANS

From the standpoint of their incidence, malignant tumors of the female genital tract constitute one of the major forms of cancer. Thus, in an analysis of 17,635 admissions for cancer at the Charity Hospital between 1928 and 1937 we find that 27 per cent of the material is made up of neoplasms of the female pelvic organs. Furthermore, a study of the 7,630 admissions for cancer of the cervix in the period 1904-1944 demonstrates a steady upward trend in the absolute number of women coming in for treatment. The high morbidity, the prolonged suffering, and the great loss in life, render this particular group of tumors of marked importance in general medicine. Fortunately, there are sound reasons for believing that alertness in diagnosis followed promptly by correct treatment can offer a very hopeful outlook. Radiation therapy has made substantial contributions to the progress in this field, and in the present report we propose to discuss the general principles of treatment observed in the irradiation of these tumors.

The, anatomic distribution of the cases seen in the Division of Therapeutic Radi-

\*Read before the Sixty-seventh Annual Meeting of the Louisiana State Medical Society, New Orleans, May 14, 1947.

†From the Department of Radiology, Charity Hospital of Louisiana at New Orleans, and the Department of Medicine of the Tulane University School of Medicine.

ology since 1938 is shown in table 1. This should not be taken as representative of the distribution in unselected material, since the

TABLE 1  
CHARITY HOSPITAL  
DIVISION OF THERAPEUTIC RADIOLOGY  
GYNECOLOGIC CANCER  
1938-1947

	No. of Cases
Carcinoma of cervix	1600
Endometrial carcinoma	98
Chorioepithelioma	12
Endometrial sarcoma	7
Leiomyosarcoma of uterus	16
Carcinoma of Fallopian tube	4
Carcinoma of vagina	33
Ovarian carcinoma	80
Other ovarian tumors	23
Carcinoma of vulva	18
Carcinoma of Bartholin gland	1
Carcinoma of urethra	6
Total	1898

cases were referred to us specifically for the purpose of receiving radiation therapy; obviously, the patients handled exclusively by operation remained in the gynecologic services. There is no doubt, however, regarding the predominance exhibited by carcinomas of the cervix. They are five times as frequent as all other tumors put together. As indicated in table 2, with variations in

TABLE 2  
RACIAL DISTRIBUTION

	Negro Per cent	White Per cent
Vulvar carcinoma	89	11
Fallopian carcinoma	75	25
Uterine sarcoma	70	30
Urethral carcinoma	67	33
Cervical carcinoma	66	34
Ovarian tumors	60	40
Endometrial carcinoma	43	57
Chorioepithelioma	42	58

the racial distribution occur, depending on the type of neoplasm, and we are impressed by the fact that, except in endometrial carcinoma and chorioepithelioma, negroes are in the majority. These features have been previously commented upon by several writers (Jeff Miller, Johnson and Tyrone, Graffagnino and McFettridge).

#### METHOD OF TREATMENT

The scope and usefulness of radiation therapy in dealing with these tumors varies. (See Table IV). The method of treatment to be chosen depends on several factors which can be defined only by discussion of the individual neoplasms. In general, both radical operations and radical irradiation, independently or in combination, can, under certain circumstances, bring about permanent control in a proportion of the cases. Emphasis should be placed on the radical concept of treatment. While it is true that we have all seen patients occasionally recover following incomplete operations and inadequate radiation therapy, it is self-evident nevertheless that the maximum achievement is dependent on rigorous application of the more extensive and thorough therapeutic procedures. In almost every instance loss of efficiency means loss of life.

The treatment of choice in carcinoma of the cervix in all forms of the disease is radiation therapy. This presupposes that the method of irradiation to be employed is capable of yielding optimum results. Obviously, a single capsule of radium inserted in the cervical canal for a period of 24 hours, more or less, does not belong in this category. The correct plan of treatment implies complete diagnosis and thorough irradiation. This includes radium application, with a field intensity of gamma radiation encompassing the whole primary tumor and its immediate neighborhood, and external x-ray therapy, administered with the intent of irradiating adequately all potential tumor sites in the lateral half of the parametria and the nodes along the pelvic wall. By complete diagnosis is meant not only that a histologic report should be available, but also that we should have full data on the anatomic extent of the disease, as far as this

can be determined by clinical examination, on the gross architecture of the neoplasm, on the degree of infection, on the status of the urinary tract, and on the existence of systemic complications and conditions that may influence the outcome of treatment. The primary morbidity and immediate mortality are greater in the presence of infection. In addition the proportion of cases salvaged is substantially lower. We know that infection is a bar to effective treatment and efforts must be made to assess its severity initially and to institute measures for its control. Fortunately, radiation itself in the form of preliminary x-ray is efficacious for this purpose and in recent years the availability of chemotherapy has constituted an important advance in the management of inflammatory complications. Fungating tumors, even though alarming in appearance, are more readily controlled than infiltrating tumors or those that have formed a crater. A urological survey is an essential step in the study of the case. The spread of cervical cancer along the parametria produces encirclement and compression of the ureters. There is some degree of obstruction present on one or both sides in about half of the cases on admission. Severe hydronephrosis and urinary infection are not uncommon findings. Presence of either or both makes the life expectancy of the patient rather brief. Treatment should be undertaken, nevertheless, since suppression of the disease remains possible. Anemia is a frequent problem and must be corrected by transfusion and medication. The age of the patient should be taken into consideration. Infection is more frequent in younger women and exacerbations of silent latent infections is not uncommon. In older women arteriosclerosis and diabetes may cause sufficient vascular changes to make full dosage unusually dangerous. The presence of syphilis seems to be an unfavorable factor. The clearest objective finding for prognostic purposes is the anatomic extent of the disease, and there is nothing more striking than the correlation between the chance for recovery and the grouping of the cases ac-



according to the League of Nations classification. Table 3 shows the results obtained in

TABLE 3  
CARCINOMA OF THE CERVIX  
JUNE 1, 1940—MAY 31, 1941  
COLORED WOMEN

	No. of Cases	Sur- vivors	Absolute five year Survival rate per cent
Stage I	7	6	86
II	39	20	51
III	62	19	30
IV	11	1	9
Recurrences and prophylactic	7	4	57
Total	126	50	40

colored patients treated subsequent to the period covered in our last report. Contrary to our former impression, we see that the absolute salvage in the negro can match the one obtained in any series of white patients whenever there is no great disparity in the quality of the initial material.

It may be stated, perhaps somewhat dogmatically, that two radium technics yield optimum results, that of Regaud and Lacassagne, or that of Forsell and Heyman, and we believe that a considerable improvement in the results of treatment would be achieved generally if either one of these technics was adopted to the exclusion of all others. Implantation of radium needles in the periphery of the cervix as a routine method is associated with greater immediate danger and a higher incidence of late complications without a corresponding improvement in the end results. The same is true of radon implants, even when an effort is made to distribute the radiation sources far laterally in the parametria. Careful physical studies have been made by Arneson, Lucas, Mayneord, Sandler, Neary, Nolan and Quimby, and others, showing that no matter how the radium is distributed in the cervix, vaginal vault, or the parametria, the amount of gamma radiation reaching the lateral half of the parametria and pelvic wall lies below the effective dosage required for the destruction of ex-

tension of the tumor in these regions. The apparent superiority of the Pitts and Waterman technic when compared with others lies in the fact that the rates of recovery for each stage apply to the Schmitz classification and not to the League of Nations classification. Interstitial radiation does have a limited field of usefulness, as in cases with complete occlusion of the cervical os, in carcinoma of the stump with a very short cervical canal, and in the treatment of recurrences. Intravaginal x-ray therapy ordinarily is a poor substitute for a good intracavity radium technic. It must be employed, however, if infection prevents radium therapy. The massive dose technic of radium therapy developed by Burman in Baltimore and Bailey and Healy in New York yield less satisfactory results and are associated with a somewhat greater incidence of undesirable sequels (late ulceration of the bladder). The value of the two preferred technics is enhanced by variation of the distribution of the radioactive foci in accordance with the individual requirements of the case, which is made possible by pre-calculation of the tissue dose. It is evident that a stenosed vagina cannot receive the same exposure in mgm. hours as a fungating tumor with a wide vaginal vault, without over-treating in the first instance or under-treating in the second instance, according to which is made the basis for comparison. The alarming recent reports as to the frequency of intestinal and bladder complications, as well as on the exhausting effects of external x-ray therapy, are consequent to the employment of technics which ignore the real purpose of x-ray therapy in combination with intracavitary radium therapy. Given adequate irradiation in the central zone of the pelvis with a radium application, the sole object of x-ray therapy is to supplement the areas of defective dosage along the lateral half of the parametria and in the region of the pelvic walls. From an analysis of the incidence of pelvic node metastasis in operative and autopsy material, it has been established that metastases occur with any degree of frequency in curable patients only

in the so-called stage I lymphatic-spread region. This includes the hypogastric nodes, the obturator nodes and the so-called principal nodes of Leveuf and Godard. Extension to the sacral nodes is rare. Invasion of the nodes of the promontory and of the lumbar nodes is beyond the scope of curative irradiation. For these reasons, external pelvic irradiation should have a restricted goal, as previously indicated, and this goal can be attained with the employment of small fields, anteriorly and posteriorly, so directed that the cervix itself, the rectum and bladder, and the femoral necks do not lie in the path of the x-ray beams. Only a small volume of intestine is directly irradiated. In this manner the incidence of primary irritative reactions in the intestinal and urinary tracts, and late sequels can be kept at a minimum; in fact, the incidence can be made negligible. Furthermore, without sacrificing the true purpose of the external treatment, the systemic effects can be reduced so that the patient, instead of becoming exhausted, improves during the course of treatment; this follows from the reduction of the total amount of energy that the body has to handle. It may be added that this technic is feasible with ordinary 200 kilovolt equipment, provided long distances and heavy filtration are employed. The required dosage need not exceed 3000 r at the tumor region when the treatment is delivered over the course of 24 to 30 days.

Carcinomas of the urethra and vagina are principally problems for radiation therapy. In relatively limited carcinomas of the urethra and vagina, control of the disease can be obtained using an interstitial radium implant by the method of Paterson and Parker and administering approximately 6000 r (gamma) in seven days. This should be supplemented by external x-ray therapy as in carcinoma of the cervix. Of the 33 carcinomas of the vagina, half were treated more than three years ago and of these seven have had three year arrest of the disease. Although the number of cases is small, this proportion of control is considerably more encouraging than the fig-

ures given in the literature (illustrative case given below).

#### CASE NO. 1

*Carcinoma of the vagina:* Mrs. J. C. W., a white female, 53 years of age, was admitted December 12, 1940 with an ulcerated mass of the posterior vaginal wall continuously infiltrating along the sacro-uterine ligaments to the hollow of the sacrum. The posterior vaginal fornix and the cervix itself were free of tumor. Biopsy showed squamous cell carcinoma. Because of the infiltration of the rectovaginal septum, a colostomy was performed following external x-ray therapy, which delivered 2000 r in air to each of six pelvic fields between December 16, 1940 and January 20, 1941. On March 18, 1941 a single plane implant was made in the posterior vaginal wall using an exposure of 1950 mghrs. of radium in a period of five days. The tumor disappeared and the patient remained well at her last follow-up visit on April 17, 1947 at which time closure of the colostomy was recommended. The survival period in this case is six years and four months.

Endometrial carcinoma occurs predominantly in women past the menopause and tends to be confined to the uterus for long periods of time. Histologically it is an adenocarcinoma with varying degrees of maturity. In cases that remain operable panhysterectomy with removal of the adnexa gives a salvage of between 50 and 60 per cent in five years. There is considerable evidence to indicate that this figure can be improved 10 to 15 per cent by combining surgery with radium therapy. It is generally agreed that the best method of managing this lesion is to introduce radium into the uterine cavity at the time of diagnostic curettage and to leave it in for an exposure of 3600 to 4000 mghrs. The surgical procedure should then be performed six weeks later, and after convalescence external x-ray therapy should be instituted. Much doubt has been cast on the utility of the radium therapy, since approximately half of the surgical specimens show residual cancer. As a matter of fact, in our own experience only nine of 30 patients showed no residual cancer. This apparent failure is difficult to interpret since patients who receive radiation alone show the same salvage rate as those treated exclusively by operation. In this connection it is well to mention that increasing the exposure to



even high levels (9000 mghrs. or more) as was done by Friedman and his co-workers is not necessarily associated with better eradication of the disease. It is necessary to consider the duration of the application, since typically adenocarcinomas are more effectively controlled by crowding of the dosage; an exposure of 4500 mghrs. for instance, may be more effective than one of 9000 mghrs. if the first is given within 48 hours and the second over a period of seven days or more. Without a doubt the Swedish school has brought the technic of radium therapy for fundal carcinoma to its highest efficiency, and report the best results.

Because of the age distribution, a considerable proportion of cases of fundal carcinoma are inoperable on clinical grounds, that is, the uterus is technically removable but intercurrent disease makes the patient unsuitable for radical surgery (marked obesity, hypertension, diabetes, or heart disease). Under these circumstances reliance must be placed entirely on adequate radiotherapy. This includes a radium application by the method of Heyman or Hurdon, followed in a month by external x-ray therapy. As previously stated, the results under these circumstances are equally as good as those of surgery alone. In a third group of cases, the disease has become too extensive for operative interference and such have to be treated by radiation, using either the combined method as for technically operable cases whenever possible, or external x-ray therapy alone, for palliative purposes. The group of patients treated by us more than five years ago is too small to give representative figures, but examples of our plan for the management of these cases are given below.

#### CASE NO. 2

*Endometrial carcinoma:* A colored female, 57 years of age, was admitted December 9, 1943 with a history of profuse vaginal hemorrhage for five days; menopause 10 years before. Physical examination revealed a well developed, obese colored female, blood pressure 210/170, the heart was enlarged outside the midclavicular line with an apical systolic murmur and occasional extrasystole was heard. The abdomen was large, no masses were palpable. Pelvic examination revealed a smooth, normal appearing cervix with a small uterus.

There was bleeding from the external os. Hemoglobin 65 per cent, RBC 3.2 million. Four days after admission a D. & C. was done. Biopsy report: papillary adenocarcinoma. The patient received radium therapy in the form of a tandem in the corpus in two applications from January 1, 1944 to January 6, 1944 for an exposure of two, 750 mghrs, and again from January 7, 1944 to January 9, 1944 for the same amount, the total exposure being 5500 mghrs. The patient was re-admitted on April 18, 1944 for a contemplated hysterectomy. At the time of laparotomy April 21, 1944 the uterus was found to be small, firm, and contained small irregular nodules. There was no evidence of extension of the tumor. A total hysterectomy and bilateral salpingo-oophrectomy was performed. On sectioning the uterus the endometrium was found to be thin, pale, and pink, there was no gross evidence of tumor. Pathologic report: leiomyomata of the uterus; chronic cervicitis; chronic salpingitis; corpora albicantia of ovaries. The patient has been followed in gynecology clinic and in orthopedic clinic where she is being treated for a hypertrophic arthritis. She remains well to date, a period of three years.

#### CASE NO. 3

*Endometrial carcinoma:* Mrs. M. W., a white female, 52 years of age, was admitted on July 20, 1942 complaining of incontinence on sneezing and coughing and urgency and burning on urination. Menopause two years before, but the month prior to admission vaginal bleeding had been experienced for one day. General physical examination revealed an obese white female who was essentially normal. Pelvic examination revealed relaxed perineum, cystocele, rectocele and urethrocele. On July 27, 1942 an anterior and posterior colporrhaphy, dilation and curettage were done. Biopsy report: Adenocarcinoma of the uterus. A radium tandem containing 45 mg. was applied in the uterine fundus from August 11, 1942 to August 13, 1942 for a total of 2250 mghrs. Reapplication on August 14, 1942, with the intention of repeating the above exposure. However, temperature rose to 102.2 and the radium was removed. Marked lower abdominal tenderness and rigidity with rebound tenderness were present and it was felt that a pelvic peritonitis was present, but the fever rapidly subsided. Four days later there was another elevation of temperature associated with a copious, foul-smelling, purulent vaginal discharge. Sulfathiazole and blood transfusions were given and the fever gradually subsided, in two weeks. At this time dilatation of the cervix revealed no pyometrium and the patient was discharged. She was re-admitted on October 8, 1942. Laparotomy on October 16, 1942 revealed a small uterus normal in size, shape and position. The right ovary was cystic and was surrounded by a large indurated mass of tissue. Areas of both the large and small

bowel were firmly adherent to the uterine fundus and because of this, it was deemed inadvisable to attempt a hysterectomy, and the abdomen was closed. Because of the patient's large size, post-operative x-ray was thought futile. She was followed in clinic and in 1944 developed abdominal swelling due apparently to ascites. This finding disappeared spontaneously, however, and the patient has remained well to date, a survival of four years and eight months following radium therapy only.

Endometrial sarcoma and leiomyosarcoma of the uterus are rather infrequent conditions but the plan of treatment is the same as for endometrial carcinoma. This is also true of chorioepithelioma, as illustrated.

#### CASE NO. 4

*Chorioepithelioma*: Mrs. R. C., a white female, 39 years of age, was admitted April 13, 1943 with complaint of bleeding for three weeks and pains in lower abdomen. She had missed her normal menstrual period in February and was told by her physician that she was pregnant. This was followed by periods of nausea and occasional vomiting. Three weeks prior to admission she began to bleed profusely and passed material which "looked like grapes." Twenty-four hours prior to admission, she had an attack of pain, bleeding and passed more of the same material. General physical examination revealed a well developed patient with no abnormalities. Pelvic examination revealed a vagina filled with blood clots, and a dilated cervical os, protruding from which was a mass of tissue in grape-like clusters. These were removed. The uterus was enlarged to the size of a five and a half months pregnancy and was very firm. Pathologic report on removed material: Hydatidiform mole, placenta with marked proliferation of syncytial cell layer. The proliferative activity strongly suggests chorioepithelioma. The patient was given several transfusions and laparotomy was performed on April 26, 1943. The uterus was found to be enlarged, smooth and somewhat soft. The ovaries appeared normal. A total hysterectomy and bilateral salpingo-oophorectomy was performed. Pathologic report: Chorioepithelioma of uterus; chronic cervicitis; ovary, corpus luteum. The patient received external x-ray therapy to the pelvis through six ports from May 24, 1943 to July 1, 1943, delivering a tumor dose of 4000 r to the lateral-borders of the parametria. The patient has been followed in clinic and has remained free of disease to date, representing a survival period of four years.

Ovarian tumors include a miscellaneous collection of neoplasms, some of which are very malignant and some rather innocent. In any event, the treatment is primarily

surgical, radiation being reserved as a supplement to the surgical procedure or as a palliative measure in cases too extensive for removal. It is considered good surgical practice in these cases to remove as much of the tumor as possible, even if the extirpation is incomplete, because considerable palliation is obtained in this manner. Although the evidence is not conclusive, it is generally considered advisable to give x-ray therapy following extirpation of the pelvic organs, unless, of course, the tumor is definitely benign. Even in the presence of widespread seeding of the peritoneum, x-ray therapy can be undertaken with the expectation of producing regression of the tumor and suppression of ascites for long periods of time.

#### CASE NO. 5

*Granulosa cell carcinoma of ovary*: Mrs. A. B., a white female, 37 years of age, was admitted May 27, 1940 with complaint of pain in the right side with nausea but no vomiting. Examination revealed cystocele, rectocele, a uterus displaced to the left and a cystic mass approximately 12 cm. in diameter located in the right adnexal region. RBC 4.2 million per cu. mm. WBC 10,000. Urine negative. On May 30, 1940 a Hegar perineorrhaphy was performed followed by a laparotomy. Exploration revealed the right ovary to be approximately 15 cm. in diameter, soft in consistency, pink in color, with a rent 6 cm. long on the posterior surface through which protruded material resembling placental tissue. A right salpingo-ooprectomy was done under the impression that the lesion was an ovarian pregnancy. Specimen revealed: granulosa cell carcinoma of ovary with areas of luteinization. X-ray was given to the pelvis through six ports (10 x 15 cm.) from June 10, 1940 to July 12, 1940: 2000 r per port. Radium therapy was given in the form of a tandem and colpostats in two applications from August 13, 1940 to August 18, 1940 inclusive for a total of 7000 mghrs. At this time the patient presented a small nodule located in the right vaginal introitus which was thought to represent an extension of the carcinoma. This was treated at the same time by means of a single plane implant for 250 mghrs. The patient has been followed in the clinic and has remained well for a period of seven years.

#### CASE NO. 6

*Bilateral papillary cystadenocarcinoma of the ovary*: N. C., a colored female, 27 years of age, was admitted October 4, 1939 with complaint of pain in the left lower quadrant present for eight months with an increase in severity during the last month. There had been no change in the nor-



mal menstrual periodicity. Abdominal examination revealed a large, firm, tender, irregular, rounded tumor mass which was felt to extend to the level of the umbilicus. Pelvic examination revealed the cervix displaced to the left, and a round tender mass in the cul-de-sac. It was felt that the patient had uterine fibroids associated with ovarian cyst. Laparotomy on October 18, 1939 revealed bilateral cysts of the ovaries. The cystic mass in the left side was the larger, extending to the level of the umbilicus. Both cysts were bound down with adhesions. Both cysts were removed, the right being ruptured in the process, with the spillage of chocolate-colored material. A supravaginal hysterectomy was done. On sectioning, both cysts were found to be lined with papillary growths. Pathologic report: Bilateral papillary cystadenocarcinoma of the ovary. The patient received external x-ray therapy to the pelvis through six ports from October 30, 1939 to January 10, 1940, receiving 2600 r per port. She was last seen in clinic in November of 1944, at which time she was doing well, representing a survival of five years.

Carcinoma of the vulva in its curable stages is a surgical problem. It occurs principally in very aged women and characteristically is a squamous carcinoma of low grade malignancy. In favorable cases a high proportion of cures can be obtained by vulvectomy, followed by inguinal dissection according to the criteria established by Taussig. These cases are rarely suited for curative irradiation, since the doses of radiation required are not well tolerated by the vulva. However, if the lesion is well circumscribed and superficial, 2nd operation is refused or inadvisable, radium therapy can be undertaken, with a good prospect for success. Dosage must be moderate. Extensive lesions, which form the bulk of the cases seen, and which are too wide-spread for curative surgery or irradiation can be benefitted by moderate amounts of external x-ray therapy. We have seen a number of very bulky carcinomas of the vulva, occurring in relatively young colored women with a long history of lymphogranuloma inguinale. These tumors are rather radio-sensitive but in most instances the disease recurs and proves fatal. A study of vulvar carcinoma at Charity Hospital has been recently completed by Dr. Arthur Lunin, of the Department of Pathology.

## SUMMARY

The relative incidence and the therapeutic principles of gynecologic cancer are discussed. The preferred plan of treatment for the various neoplasms is presented with illustrative case histories. Results obtained in the treatment of carcinoma of the cervix in the negro are reported.

TABLE 4  
GYNECOLOGIC CANCER

	Surgery and radiation Per cent	Radiation Alone Per cent
Vulvar carcinoma	17	83
Carcinoma of fundus	57	43
Ovarian tumors	57	43
Chorioepithelioma	67	33
Uterine sarcoma	70	30
Fallopian carcinoma	100	---

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## INFECTIOUS HEPATITIS AND HOMOLOGOUS SERUM JAUNDICE

### THE SAME OR DIFFERENT DISEASES

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NEW ORLEANS

#### INTRODUCTION

Infectious hepatitis, known also as infective hepatitis, epidemic catarrhal jaundice, common infective hepatitis, jaundice, non-spirochetal infectious jaundice, campaign jaundice, catarrhal jaundice, ictère contagieux, jaunisse de champs and Kreigsicterus, is a well known affliction of armies in the field and particularly prevalent during times of war.

During World War II, jaundice was a major medical problem among the troops of the allies.

Now, either due to increased consciousness of the possibility of infectious hepatitis or homologous serum jaundice in jaundiced patients, or due to an actual increase in the morbidity of the aforementioned diseases, the diagnosis is frequently made. Because of the great interest, as well as confusion, existing concerning these two diseases, and in the hope of creating some order out of the immense volume of literature on this subject, this paper is written.

#### NATURAL HISTORY

In a recent paper by Lucke, reference is made to epidemics of the disease in foreign armies in the Franco-Prussian War, in the South African wars and in World War I.

In the American Civil War there were over 50,000 cases and 231 deaths among

Union troops and a small epidemic occurred in our Army of Occupation in 1919.

In 1934, incidences of jaundice following inoculation with yellow fever vaccine were observed. Jaundice was thought to be a coincidental or superimposed feature. Normal human serum was being used at this time as a vehicle during desiccation for the neurotropic strain of yellow fever virus, then employed as a vaccine.

In 1936 and 1937, when using the attenuated pantropic yellow fever virus strain #170, with and without additional injections of human immune serum, further instances of jaundice occurred, the cases being so numerous they could no longer be considered coincidental.

In 1937 and 1938, Findlay and MacCallum demonstrated that the icterogenic agent had no relation to the strain of yellow fever virus used, but that it was derived from the human serum used in the preparation of the vaccine.

They further demonstrated that the agent had many of the properties of a virus by heating the serum to 56° C. for 30 minutes and filtering through a Seitz filter before use and producing jaundice in those inoculated.

It is the purpose of this paper to compare the two diseases, infectious hepatitis and homologous serum jaundice, to point out their similarities and dissimilarities in an attempt to establish the unicity of each disease or the close kinship of the two, and thus to aid the reader in reaching a conclusion concerning the homogeneity or heterogeneity of the two and also to express my conclusions.

The quest for the solution to the problem posed by this paper is further complicated by the fact that the etiologic agent (or agents) of the two diseases has never been satisfactorily isolated and demonstrated conclusively. It is perhaps redundant at this point to remark that were the etiologic agent (or agents) isolated and demonstrable, the problem would be solved and the necessity for this paper obviated.

I shall trace the natural history, epidemiological, clinical and biochemical aspects of



the disease in order to demonstrate the likenesses and differences in the two diseases since, lacking other essential data, this method although tedious is nevertheless essential.

Experimental data are sparse and quite repetitious. However, since it is only through well conducted experiments that a solution is to be reached, it is hoped that new lines of investigation may be pointed out by the inquiries and surmises of this paper.

#### EPIDEMIOLOGIC ASPECTS

Walker, in his investigation of the epidemiology of infectious hepatitis and homologous serum jaundice in the United States Army in 1942, found that the incubation period was around 30 days for infectious hepatitis and two to four months for homologous serum jaundice.

Homologous serum jaundice had a low degree of communicability, while infectious hepatitis was more highly communicable.

One outbreak of jaundice in the Army had been preceded by vaccination for yellow fever two months previously.

In 1943, Findlay and Martin produced mild jaundice in human volunteers by instilling into their noses the nasal washings of three patients from the North African theatre in the pre-icteric and early stages of hepatitis following yellow fever immunization. Apparent transmission of the two diseases in this manner will be further discussed under experimental aspects of the diseases.

The apparent restriction of the disease in North Africa to certain insect-ridden areas plus the tendency of incidence curves toward a relationship with those of malaria and sandfly fever, but occurring three months later, led observers to the belief that infectious hepatitis is transmitted by blood-sucking insects and that the prolonged incubation period that obtains in post-vaccinal hepatitis also obtains in the naturally occurring disease. Furthermore the virus of infectious hepatitis is proved by experiments to occur in human feces. It is spread under conditions that favor the

spread of bacillary dysentery. Frasher and Hallgren report cases due to contamination of drinking water.

In the same epidemic it was found that the highest incidence of cases occurred in October and November.

This same investigator found in studying the epidemiology of infectious hepatitis in the British Army in Sicily in 1943 and 1944, that the disease followed dysenteries most frequently by two to three months. The most likely explanation is that the conditions which favored the spread of the other infection also favored the spread of infectious hepatitis.

The orthodox belief that infectious hepatitis is spread by droplets from the respiratory tract is supported by the autumn-winter incidence of the disease in Sweden, Great Britain and the Mediterranean area as is also the apparent transmission of the disease by casual contact.

The indescribable filth and plague of flies in the Alamein line and the constant inspiration and ingestion of all prevailing dust were features of the life of troops in 1942 which suggested that feces, flies and dust might have played a part in the spread of the infection. Lack of water and washing facilities also increased the risks of spread by fingers contaminated by droplets or feces.

Findlay and Martin, in further investigations, reported that climate, physical strain, diet and alcohol seemed to have no influence on the attack rate.

Younger men were usually affected. Air crew members as a group seemed to have the greatest number of cases. Among these the attack rate among officers was greater than the attack rate among enlisted men. The fact that they ate in a common mess where communal dishes were used which were washed together, while the men ate out of their own utensils and, theoretically, each used his own, further substantiates the opinion that contact is the mode of spread of infectious hepatitis. The higher incidence among officers in the Mediter-

ranean area may have been due to increased opportunities for contact.

Homologous serum jaundice follows the parenteral injection of blood or blood products usually by six weeks to six months. As little as 0.01 c.c. of plasma introduced parenterally has been known to produce the disease. As far as is known, no other mode of transmission is present.

The British Ministry of Health attributes 48 cases of jaundice with eight deaths to the use of pooled convalescent serum and adult human serum for measles. The incubation period varied from 16 to 161 days.

The blood group and Rh factor have no relationship to susceptibility as was proved in 12 cases following transfusion.

The icterogenic serum was examined with an electron microscope and showed no particles of uniform morphology.

Parr, investigating homologous serum jaundice in the Army under the unique conditions of control which existed in the armed forces as far as the nature and "invasion" of the etiologic agent are concerned, found the incubation period in different epidemics to vary as follows:

Site	Incubation Period	Extremes
Fort Custer	104 days	88-121 days
Camp Polk	96 days	85-106 days
Iceland	99 days	79-140 days

These incubation periods were measured from time of inoculation to onset of jaundice and no consideration for subclinical, non-icteric states was made. As will be shown later, hepatic damage may precede the onset of jaundice by many weeks so that one must be cautious in interpreting incubation periods as determined above.

Booth and Okell found in their investigation of cases of jaundice in England that cases following yellow fever virus inoculation or measles convalescent plasma always developed between 60 to 100 days after inoculation.

The incubation period of the naturally occurring jaundice was between 20 and 40 days. From evidence collected the cases were probably infectious in the pre-icteric stage and the disease was spread via drop-

let infection. Booth and Okell surmised that differences in the portal of entry may be responsible for difference in the incubation periods of the two diseases.

Neefe, Miller and Charnock state that in investigating homologous serum jaundice they were led to the belief that the causative agent is a virus by the fact that it was invisible under the microscope, it passed through bacteria-retaining filters, it persisted in serum-chick-embryo media, and was resistant to procedures that ordinarily kill vegetative bacteria.

Findlay, Martin and Mitchell, in a series of investigations were convinced that the only point of clinical difference between infectious hepatitis and homologous serum jaundice is in the supposedly longer incubation period in infectious hepatitis following yellow fever inoculation; an average of 100 or more days, as against 20 days for infectious hepatitis.

Turner, Snavelly et al., studying acute hepatitis occurring in soldiers at Camp Polk, after inoculation with yellow fever vaccine, found the incubation period to vary between nine and 23 weeks. Fifty per cent of the cases developed symptoms during the fourth month after inoculation; 52 per cent were admitted during the first week of illness; 41 per cent during the second week and 7 per cent from the fourth to the ninth week.

Hoagland and Shank, in a review of 200 cases of infectious hepatitis, found the acute febrile period was preceded by prodromal symptoms two to six days before the onset of icterus. In contrast to the corresponding period in homologous serum jaundice this seems to be enough evidence to warrant a differentiation in the two illnesses. However, as will be shown later, many factors affect the incubation period and one must not mistake their effect upon the incubation period as a property of the virus *per se*.

Infectious hepatitis affects the greatest number of persons in the fall and early winter. This has been borne out by the epidemi-



ological studies of many investigators, chief among whom is Gould.

#### CLINICAL PICTURE

Infectious hepatitis and homologous serum jaundice present a clinical picture which makes it impossible to distinguish one from the other. This has accounted for much of the confusion existing about the two diseases. The only way to differentiate the two is through the determination of the incubation period together with a history of previous inoculations or transfusions with human blood or serum or derived products.

Nausea, vomiting, right upper quadrant pain or distress, headache, and not uncommonly, diarrhea, are among the first symptoms.

Icterus usually appears on an average of five days after the onset. The height of the icterus is not proportional to the clinical symptoms; the icteric index varies from 12-15 in the subicteric cases and to 220 in the severely jaundiced patients. Liver tenderness and hepatomegaly occur in about 60 per cent of the cases. The red cell count is normal as is also the hemoglobin and white cell and differential count. Leukocytosis is rare. Hematuria and back pain may occur late. The period of disability varies from 21 to 90 days and averages 35 days.

Some observers report the onset as occurring with acute chills and fever and mild prostration together with the aforesaid symptoms. The more usual picture is that of a patient who feels perfectly well one day, arising the next day with a marked anorexia, headache, and upper respiratory symptoms. These lead him to believe he is developing a cold until four to six days following the onset of symptoms he becomes jaundiced.

Again to quote Turner in his investigations of homologous serum jaundice at Camp Polk: anorexia occurred in 77 per cent of the patients, weakness in 58 per cent, abdominal pain or distress in 32 per cent and vomiting in 20 per cent.

Other early symptoms were malaise, joint and back pain, urticaria, burning of

the eyes, lassitude and headache. A palpable tender liver was the most common sign other than the icterus.

The signs and symptoms of hepatitis following inoculation with homologous serum products differ in no way from those of infectious hepatitis.

The laboratory data on such cases will be mentioned later. Liver function tests show the presence of liver damage in the case of both types of jaundice, the icteric index is elevated and other routine laboratory studies are within normal limits.

Albuminuria and isosthenuria, massive hemorrhage into the gastrointestinal tract, ascites, rashes, and petechiae together with anemia are the most frequent complications of both homologous serum and infectious hepatitis.

Epidemiology is, thus, the only distinguishing feature of infectious hepatitis and homologous serum jaundice.

Klatskin and Rappaport investigated residual liver damage due to homologous serum jaundice and infectious hepatitis: 217 patients considered fully recovered from one or both of the diseases had residuals evidenced by symptoms, hepatomegaly or impaired liver function for periods ranging up to 27 years. The only significant symptoms were fat intolerance and right upper quadrant pain.

The duration and severity of the jaundice were the significant factors in the incidence of residuals varying directly with the incidence of residuals. The residuals were compatible with good health and activity over long periods of time.

#### BIOCHEMICAL ASPECTS

The biochemical aspects of infectious hepatitis and homologous serum jaundice have been investigated but little. In the voluminous literature on the two illnesses, however, the following summarizations may be made:

Numerous laboratory tests show no difference in the picture presented by infectious hepatitis and that presented by homologous serum jaundice. An increased icteric index is common to both. The leukocyte

count rarely exceeds 12,000 and rises from a leukopenia in the febrile and pre-icteric stages to this level in the icteric stages. There is a relative lymphocytosis during the leukopenic stage.

Greenblatt and Kaplan report target cells that have an increased resistance to hypotonic saline solution during the acute stages of infectious hepatitis. The erythrocyte sedimentation rate is only occasionally elevated.

Hayman reporting on an outbreak of jaundice following yellow fever vaccination states that in 398 cases the differential count was normal.

Finks and Blumberg found hepatic function, as measured by the synthesis of hippuric acid, seriously impaired as long as two months after the icteric index returns to normal.

Turner et al. state that liver damage as indicated by the icteric index, prolonged prothrombin time, hyperbilirubinuria, albuminuria, the Hanger flocculation test, darkened urine, galactose tolerance tests, pale stools, and decreased plasma proteins, point to a failure of three and possibly four liver functions: (1) Ability to elaborate an external secretion such as bilirubin and cholic acid; (2) synthesis of prothrombin, albumin, cholic acid, and glycogen from galactose, and (3) failure to supply a vascular channel between splanchnic vessels and vena cava.

Oliphant in 1944 found that the leukocyte count, differential count and Schilling count showed no significant changes during the period of jaundice of homologous serum type.

Many investigators have reported on laboratory tests in homologous serum jaundice and infectious hepatitis and the results are all indicative of hepatic damage of varying degrees of severity.

Pathologic data on the fatal cases of both homologous serum jaundice, and infectious hepatitis are scarce.

Subacute central necrosis of the liver, massive gastrointestinal hemorrhage, ascites, rashes and petechiae are common to

all fatal cases. The latter findings can all very well be attributed to the liver damage.

Havens, Paul and Sabin, in a series of studies provided evidence of a decreased susceptibility of the general population of ages greater than 35 years to infectious hepatitis. They believed this to be due to subclinical infection during early life.

This was borne out by the demonstration of antibodies in human immune serum globulin prepared from large pools of normal human plasma which have been proved to be effective against the virus of infectious hepatitis.

Stokes, Neefe, Gillis, Brother, Hall, Gilmore, Keefer and Morrissey, Havens and Paul, working separately and in groups recommended the use of human immune serum (gamma globulin) in the prevention and treatment of infectious hepatitis.

Hoagland and Shank believe that plasma bilirubin determinations, the ratio of free to total cholesterol and the plasma retention of sulfbromphthalien are the most useful and unequivocal tests agreeing with the severity of the clinical findings.

Liver tests, in general, seem to be most valuable during convalescence when it is not possible to determine whether or not convalescence is complete.

Klatskin and Rappaport, in investigating late residuals in presumably cured infectious hepatitis found residuals of liver damage which, however, were compatible with good health and activity and there is some doubt that the liver damage they describe was not present before the attack of infectious hepatitis or acquired after the attack as the result of factors unrelated to the hepatitis.

Lucke believes the restoration of liver structure is complete in all cases and criticizes Klatskin and Rappaport in the same manner and for the same reasons presented above.

Barker describes a group of patients with persistent symptoms, signs and impaired function following an attack of acute hepa-



titis who characteristically relapse when exercise is taken.

Briskin presents evidence that impaired liver function may exist without gross or microscopic changes as is demonstrated by failure of the liver to inactivate estrogen when injured by vitamin B deficient diets.

It is of interest to note that the suggestion has been made that ultraviolet light may prove effective in inactivating the causative agent of homologous serum jaundice in pooled sera. However, the amount of radiation necessary to destroy the agent is very near that amount which will not leave unchanged the essential properties of serum. The usefulness of the whole serum or gamma globulin is destroyed by the temperature necessary to inactivate the agent although the albumin fraction may be able to survive this temperature.

Janeway and Paul point out that the etiologic agent of infectious hepatitis or homologous serum jaundice has never been seen, cultured or transmitted to laboratory animals.

Herein lies the problem now facing medical research.

#### EXPERIMENTAL DATA

Here lies the key to the problem: As in all subjects in which the medical profession occasionally indulges itself by the writing of many articles for current literature, this phase is scarce in relation to the accumulation of other data.

In the belief that only through accurate, carefully executed and intelligently analyzed experiments can the reader chart a course through the sea of speculation in which he finds himself, which will bring him to plausible conclusions, this paper will dwell at length upon this aspect of homologous serum jaundice and infectious hepatitis.

Neefe, Stokes and Gellis reported in 1945 the production of homologous serum jaundice in the human volunteers by the parenteral administration of materials known to contain a causative agent of this disease. After recovery the six men were inoculated parenterally with a plasma containing the

causative agent for homologous serum jaundice to test for homologous serum jaundice immunity.

Concomitantly, nine normal control subjects without history of either infectious hepatitis or homologous serum jaundice were inoculated parenterally with the same plasma. None of the six men in the test group developed incapacitating symptoms or jaundice, whereas eight of the nine control subjects developed hepatitis with jaundice. The six men were then inoculated, one orally and five parenterally with materials known to contain a causative agent of infectious hepatitis to test for cross immunity. Twelve normal controls with a history of hepatitis also were inoculated with these materials, six orally and six parenterally.

Of six men tested for cross immunity five again developed hepatitis, evidence being conclusive in four and very suggestive in the fifth. The one not developing hepatitis had had both infectious hepatitis and homologous serum jaundice previously. Five of six controls inoculated orally developed hepatitis. None of the six inoculated parentally developed hepatitis.

The interval between inoculation with homologous serum jaundice agent the onset of jaundice usually exceeded 60 days. The time between inoculation with infectious hepatitis agent and onset of jaundice did not exceed 37 days regardless of the route of inoculation.

The oral temperatures in homologous serum jaundice did not exceed 100° F. regardless of the route of inoculation. The oral temperatures in infectious hepatitis exceeded 100° F. regardless of the route of inoculation.

To summarize these data the following conclusions are reached:

1. There is a lack of cross-immunity between serum jaundice and infectious hepatitis.
2. A batch of pooled human serum containing the causative agent of homologous serum jaundice produced jaundice in 40 per

cent of those inoculated with it. Inoculation of volunteers with the same serum itself produced hepatitis and jaundice in a similar percentage.

3. The icterogenic agent survived heating at 56° C. for one hour and was still active after storage for 14 months in the dried state.

4. A number of those injected with the icterogenic agent showed evidence of liver damage of insufficient severity to produce jaundice.

5. Results obtained on two volunteers are not incompatible with the view that the icterogenic agent present in the blood in homologous serum jaundice is capable of multiplying in tissue culture.

Neefe, Stokes, Reinhold and Lukens, in experiments using nine white male volunteers between the ages of 18 and 25, reported the following results: Incidence, 10 out of 10 volunteers.

Icterogenic Material	Number Inoculated	Hepatitis with Overt Jaundice	Hepatitis without Jaundice		Negative Results
			Definite	Probable	
Plasma 'A'	6	5			0
Plasma 'B'	2		2	1	0
Yellow fever virus Lot 335	2	1	1		0

These volunteers had: (1) No significant medical history or physical abnormalities; (2) normal red and white cell counts, normal red blood cell fragility, urinalysis and serology; (3) normally functioning gall-bladder; (4) no evidence of hepatitis disturbance.

The clinical courses were as follows: (1) Mild symptoms and signs appeared 12 to 35 days after inoculation; (2) these symptoms and signs abated and an asymptomatic interval or interval with periodic recurrences of mild symptoms and signs followed which after 73 to 110 days culminated in clinical jaundice. The course thereafter was similar to that of infectious hepatitis; (3) hepatitis was present long before jaundice occurred.

Thus, Neefe et al. found that the first signs of hepatitis following inoculation with serum products containing homologous se-

rum jaundice agent appeared in 12 to 35 days after inoculation.

Previous estimates of the incubation period had been 60 to 100 days. Could not the true incubation period be 12 to 35 days? Paul, Havens, and Sabin in transmission experiments with serum jaundice and infectious hepatitis found that infectious hepatitis can readily be produced in man via the oral routes. This can be accomplished by feeding infective feces or by spraying such material into the nasopharyngeal passages. Similarly the disease can be produced by feeding infective serum as well as by its parenteral administration.

These experiments are in close agreement with the epidemiologic aspects of an epidemic of hepatitis reported in a children's summer camp in Pennsylvania in which the infective agent was demonstrated to be present in the well water of the camp. Thus, it is definite that the agent of infective

hepatitis is present in the feces and possibly in the urine.

Findlay and Wilcox found the transmission of infectious hepatitis to take place via the feces and the urine. With the exception of one report by Oliphant all investigators are in agreement on the route of transmission as presented above.

McCallum and Bradley found the virus in the feces and that the disease can be induced after a 20 day incubation period, by feeding such material to arthritic patients who volunteered for these experiments.

The infective material was collected from several patients in the early stages of infectious hepatitis. Two of three volunteers developed the disease in 20 to 22 days after having been fed such material.

Havens, Ward, Drill and Paul further reported that the serum taken from two



patients with infectious hepatitis in the preicteric stage was filtered and immediately heated to 56° C. for 30 minutes. This heated serum filtrate produced infectious hepatitis in four out of five human volunteers with an incubation period ranging from 20 to 31 days.

Some of the latter group of volunteers had recovered some months before from homologous serum jaundice but this apparently did not protect them against an attack of infectious hepatitis. Thus, with this strain of virus jaundice hepatitis was produced in six of 11 subjects when the virus was inoculated and in six of eight subjects when the virus was fed. The incubation period was invariably less than 34 days in these experiments.

Findlay and Martin demonstrated that when postnasal inoculation is used to transmit hepatitis to man the incubation period is 28 to 50 days.

One might conclude that the alleged difference in the incubation period in homologous serum jaundice and infectious hepatitis seems to be associated with the route of inoculation and is not necessarily a real difference due to disparity in the agent of the two diseases.

An antigen made with the livers of patients dying with infectious hepatitis fixes complement with the sera of patients who have recovered from infectious hepatitis and from post-inoculation hepatitis.

Neefe, in a series of experiments with the causative agents of homologous serum jaundice and infectious hepatitis, reached the following conclusions substantiated by his experiments:

1. Persons previously infected with the virus of homologous serum jaundice were more susceptible as a group to parenterally infected virus of infectious hepatitis.

2. Persons previously infected with the virus of homologous serum jaundice were not protected from infection with the virus of infectious hepatitis.

3. Men with resistance to a second inoculation with the virus of homologous serum

were not resistant to infection with the virus of infectious hepatitis.

4. Men recovered from infectious hepatitis could not be infected with the virus the second time.

5. Men recovered from homologous serum jaundice could not be infected with the virus a second time.

6. Infection with homologous serum jaundice provided no immunity to infectious hepatitis and vice versa.

7. Parenteral injection of infectious hepatitis agent gave resistance to infectious hepatitis as acquired by the oral route suggesting a method of immunization.

8. Two persons were not resistant to homologous serum jaundice virus four and 10 years respectively after so-called "catarrhal jaundice."

9. Two persons were resistant to infectious hepatitis virus five and 18 years respectively after an attack of "catarrhal jaundice."

10. Virus producing infectious hepatitis in Sicily gave protection against the virus producing infectious hepatitis in Pennsylvania.

However, this strain was reported by Havens and Paul to produce hepatitis effectively by the oral or parenteral route of administration.

Havens, studying the period of infectivity of patients with experimentally induced infectious hepatitis found the "virus" in the serum in the acute phase of the disease but not midway through the incubation period or in the serum or stools in the convalescent period of infectious hepatitis.

In homologous serum jaundice the presence of the virus has been demonstrated one-third and two-thirds through the incubation period in human volunteers.

Further substantiation was afforded by other experiments in which pooled specimens of urine and nasopharyngeal washings obtained from five patients in the acute phases of infectious hepatitis when the virus was proved to be in the stools and serum were fed and given intranasally to

six volunteers. Infectious hepatitis was not produced in any of the volunteers.

For other experimental data the reader is referred to the bibliography.

The data as given above summarize and typify the similarity and differences between homologous serum jaundice and infectious hepatitis.

Other experiments are merely repetitions of the data as obtained by the experiments discussed above.

#### DISCUSSION

Many conclusions are possible from the data obtained.

In a recent editorial in the *Lancet* the possibilities tentatively presented were:

1. Infectious hepatitis and homologous serum jaundice are due to one and the same virus.

2. Different agents produce the same clinical picture but are not mutually protective. This may be similar to the condition prevalent in influenza in which "A" type virus and "B" type virus produce the same clinical picture but are not mutually protective.

3. Different strains of the same virus which are antigenically related produce the diseases. However, these possibilities leave out one of the most important ones: one which seems increasingly possible in the light of recently accumulated data, namely

4. The two diseases are produced by entirely different and unrelated agents which principally affect the same systems and organs wherein lies their only similarity.

This paper by title proposes two possibilities: (1) the diseases are the same or (2) they are different as regards etiology.

One is compelled to define the terms used here in order to avoid confusion.

By different etiologies is meant etiologies due to different agents. Whether or not they are both bacteria or viruses makes no difference for just as bacteria are of many and varied kinds so are viruses.

There is no argument when one states that the virus of yellow fever differs from the virus of influenza. This is a proved

known recognized fact. Then is it not conceivable that homologous serum jaundice and infectious hepatitis are caused by different viruses?

Since a virus is submicroscopic in size, methods to prove the existence of such have revolved about the study of the antigenic properties of the virus.

Its ability to produce the same clinical picture in subsequent victims, the uniqueness of its epidemiology and its ability to stimulate the formation of protective antibodies in the individual affected which protect against subsequent attacks are vital tools in its differentiation from other viruses.

The least important of all the above mentioned criteria is the ability to produce similar clinical pictures in subsequent victims.

Any illnesses attacking the same organ can produce similar clinical pictures and upon this premise in the light of other differences found it is the essayist's opinion that homologous serum jaundice and infectious hepatitis are different diseases related only in similar clinical pictures and in that each is caused by a virus.

What proof is there to support this conclusion?

1. Incubation period of infectious hepatitis is approximately three weeks; that of homologous serum jaundice is approximately three months.

2. Infectious hepatitis is transmitted via the gastrointestinal tract and homologous serum jaundice to date has not been transmitted except via parenteral inoculation.

3. The causative agent of infectious hepatitis is present in the feces of persons with this disease and produces the disease when administered orally. The causative agent of homologous serum jaundice has never been demonstrated in the feces of persons suffering with this disease.

4. The transmission of the causative agent to other persons via means other than injection of blood products is common with infectious hepatitis and rare with homologous serum jaundice. Findlay and Martin in 1943 reported the transmission of what they believed to be homologous serum jaun-



dice by nasopharyngeal washings. MacCollum and Bradley had only doubtful success with similar material from homologous serum jaundice cases. The weight of evidence seems to favor the view that homologous serum jaundice is produced only by the parenteral injection of blood products.

5. Homologous serum jaundice does not spread from patient to patient under conditions favoring the spread of upper respiratory infections and bacillary infections as does infectious hepatitis.

6. There is a lack of cross immunity between homologous serum jaundice and infectious hepatitis. This was very effectively proved by Paul, Havens, Sabin and Phillip.

7. Gamma globulin protects against infectious hepatitis and apparently is ineffective against homologous serum jaundice.

8. The mortality in homologous serum jaundice seems higher than in infectious hepatitis.

9. Fever and upper respiratory infections are more frequent with infectious hepatitis than with homologous serum jaundice. Also there is characteristic second wave of jaundice in infectious hepatitis which does not occur with homologous serum jaundice.

10. An attack of either illness confers an immunity against a second attack of the same nature but as mentioned before, not against the other illness. Cameron reports that a second attack of infectious hepatitis is not uncommon in Palestine where the disease is endemic. However, experimental evidence is strongly against this and lacking more convincing evidence we must assume that second attacks do not occur.

11. Clinically, an attack of homologous serum jaundice is more severe than an attack of infectious hepatitis. The occurrence of fever, however, is a questionable means of distinction.

Looking at the problem from another viewpoint Oliphant very logically believes that minor differences in the clinical manifestations may exist because of: (1) Differences in the portal of entry of the agent; (2) conditions under which the agent or agents have existed prior to entry, as for

example, the desiccation of the blood products incident to their use in serums; (3) the possible presence of immune bodies in the hepatitis-producing serum or plasma pools that may be temporarily protective.

To quote Oliphant, he sums up his conclusions by stating: "Thus the length of the incubation period, the clinical phenomena and the pathological changes do not appear to provide a satisfactory basis for distinguishing between the etiologic agents of these diseases. The only logical difference seems to be the tendency of the epidemic type of hepatitis to spread among contacts."

Findlay and Martin following the same line of reasoning concluded that infectious hepatitis and homologous serum jaundice are due to the same or very closely related agents.

They believed that patients who have had an attack of infectious hepatitis have some although not complete immunity against homologous serum jaundice and presented some evidence in support of this view.

The authors supporting the view that the diseases are due to the same agent, however, have not overcome the chief and most convincing obstacle in the pathway of such a view.

The lack of cross immunity between the two diseases while each produces immunity against itself is much too strong a bit of evidence to be put aside lightly.

Many attractive theories, among which one has been mentioned in this paper, have been presented to account for the lack of cross immunity between the two diseases.

To support these theories other unusual and at times unlikely theories must be forwarded. On the other hand the premise that the two diseases are due to different etiologic agents necessitates no such theorizing.

Sodeman, in a review of the literature, states that two chief differences rest in the incubation periods and the epidemiology of the two diseases.

Without becoming emotionally attached to one or the other views and weighing the evidence for and against each one as the evidence is now available, the weight of evi-

dence is heavily in favor of the view that homologous serum jaundice and infectious hepatitis are due to entirely different etiologic agents. This statement must be qualified by saying that new evidence may be presented in the future that will make this conclusion untenable.

Until that time, however, in view of the evidence as presented in this paper, I am unequivocally in favor of the premise that the two diseases are different.

#### CONCLUSION

I feel compelled to acknowledge the fact that this paper does just what it criticizes other papers for doing: contributing nothing new in the way of experimental evidence.

Nevertheless two viewpoints have been considered in, it is hoped, an unbiased manner and a logical conclusion has been reached.

One would not be so conceited as to say this is the final conclusion but only that it is the most likely conclusion in our present state of knowledge.

#### SUMMARY

1. The natural history, epidemiology, clinical and biochemical, as well as experimental aspects of homologous serum jaundice and infectious hepatitis have been compared.

2. Their differences and similarities have been stated and discussed.

3. The conclusion is reached that homologous serum jaundice and infectious hepatitis are different diseases due to different etiologic agents.

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- analyzed in detail elsewhere.<sup>1</sup> Since the preliminary report, however, additional information has been gained and several reports by others have appeared. Hoffbauer,<sup>2</sup> who summarized his later experiences, stated that he had had no further difficulties than the previously reported case of hemorrhage. Gillman and Gillman<sup>3, 4, 5</sup> describe a series of 500 biopsies with only one death from hemorrhage. Mallory and his coworkers<sup>6</sup> had considerable experience with the procedure in the Mediterranean theatre in connection with epidemic hepatitis. With increasing familiarity with the technic, the risk becomes minimal.

The first method of liver biopsy to have been employed extensively was performed by the introduction of a small bore needle into the liver with or without the previous administration of an anesthetic and aspiration of a few cells with a small syringe. These were expressed onto a slide smear and examined directly and again after staining with the Romanovsky dye. This method carried little or no risk but the information it supplied was minimal. It has largely been discarded.

The method commonly in use at present consists in the introduction of a trocar about 2 mm. in diameter and either aspiration or compression extraction of a core of tissue. Approach has usually been through the ninth interspace in the posterior axillary line or below the right costal margin, though mid-axillary and anterior axillary approaches have also been used. European proponents of the technic have almost all used the intercostal approach and they have had by far the majority of deaths.<sup>7, 8, 9, 10, 11</sup> Liver biopsy was first introduced in New Orleans by Tripoli and Fader.<sup>12</sup> They reported 14 biopsies done with the Silverman needle by the anterior subcostal approach without complications.

The series to be reported has been divided into two groups for purposes of comparison. The first group consists of biopsies done from 1939 to July 1, 1943 when no special instruments were used and the second group comprises all biopsies done from July

## NEEDLE BIOPSY OF THE LIVER\*

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NEW ORLEANS

This paper is based on observations of a series of 128 needle biopsies of the liver done on patients admitted to the Cleveland City Hospital and the Ochsner Clinic from 1939 to 1947. The first 79 of these were

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1, 1943 to April 10, 1947 with the Silverman<sup>13</sup> or Roth-Turkel<sup>14, 15</sup> needles.

The Silverman instrument employs a split inner needle; it is introduced through a trocar and thrust beyond the trocar into the tissue enclosing a small core between its prongs. The trocar is then advanced, compressing and freeing the core of tissue and the whole is withdrawn.

The Roth-Turkel needle, on the other hand, consists of an outer trocar with stylet and an inner hollow needle with small saw-teeth at the end. The trocar is introduced to the surface to be examined and the stylet removed; the inner needle is inserted, slowly advanced and rotated back and forth to cut out a core of tissue about 2 mm. in diameter. After the proper depth has been reached, the needle is rotated several times in a clockwise direction to free the core and then withdrawn as negative pressure is maintained with an attached 20 c.c. syringe. The specimen obtained is usually 0.2 cm. x 2 cm. to 3 cm.

Biopsy is done at the bedside with ordinary sterile precautions and procaine infiltration anesthesia which is carried down to include Glisson's capsule, if possible. Further exploration is done with a long 22 or 25 gauge needle to obviate the possibility of entering a large blood vessel or a collection of pus with the trocar. The skin is incised with a bistoury and the biopsy accomplished, the needle usually being directed upward and to the right toward the center of the liver. Approach is usually through the right subcostal region a few centimeters to the right of the xiphoid process unless there is a specific nodule to be transfixed. A pressure dressing is applied and the patient is allowed full activity. Little pain is experienced; one dose of analgesic immediately after biopsy is usually sufficient. In the more recent biopsies the patients have not complained of pain even the next day. As a precaution blood pressure and pulse rate are checked at frequent intervals for the first few hours following the procedure. Routine bleeding, clotting and prothrombin times are determined preoperatively. Biopsy is contraindicated in

the presence of uncontrollable hemorrhagic tendency.

It is felt that the presence of significant ascites is an additional hazard in that approximation of visceral and parietal peritoneum may be prevented. Biopsies should then await removal either by diuretics or paracentesis. Risks of biopsy include hemorrhage into the peritoneal cavity or abdominal wall; perforation of nearby viscera, such as the large or small intestine, gall-bladder, common duct or hepatic duct; the introduction of infection or the spread of localized infection. In our series of 128 biopsies the only complication was one severe hemorrhage. The patient succumbed about 24 hours after the biopsy was done and at autopsy it was discovered that approximately 500 c.c. of blood had been lost. In view of the severe hepatic damage, biliary nephrosis and absence of shock before death it was the opinion of the pathologist that the cause of death was hepatic and renal failure rather than hemorrhage. In 22 autopsies and one peritoneoscopy, no evidence of serious damage other than the case of hemorrhage was found.

Table 1 shows the number of biopsies done during the two periods with the degree of success. The concomitant increase in the number of biopsis and percentage of success are easily seen. Biopsies were considered successful if sufficient tissue was obtained for pathologic study.

TABLE 1  
COMPARISON OF SUCCESSFUL AND HELPFUL  
BIOPSIES FOR PERIODS 1939-1943 AND  
1943-1947

Group	Biopsies	Successful	Per cent	Helpful	Per cent
I-1939-1943	26	16	61.5	13	80.0
II-1943-1947	102	93	91.2	79	85.0

The relative frequency of diagnosis is shown in table 2. These have been reported by many different pathologists and their diagnoses are unaltered though the slides have since been reviewed. There is a striking difference in the relative frequency of both the diagnostic and the unsuccessful biopsies before and after the introduction of the



special needles. Contrary to the early group the diagnosis of cirrhosis has now become the most common and with the almost invariably good specimens now obtained and accurate autopsy check the diagnosis of "consistent with Laennec's cirrhosis" has been discarded. Criteria for the diagnosis of cirrhosis include perilobular fibrosis, bile duct regeneration, alteration of lobular architecture and invasion of the lobules by fibrous tissue. The diagnosis of carcinoma includes all slides in which the diagnosis of malignant neoplasm was made. The diagnosis of fatty metamorphosis was at times a primary one but in many cases of tumor or cirrhosis it was a secondary one. The classification of acute hepatitis includes both periportal and diffuse types. The unsatisfactory cases are those in which sufficient tissue was lacking for histologic diagnosis. Of the nine unsatisfactory biopsies in the later group, three were in patients who subsequently had satisfactory biopsies and one was a small child whose lack of cooperation made biopsy impossible.

TABLE 2  
FREQUENCY OF DIAGNOSIS

	1939-43	1943-47	Total
Cirrhosis	1	32	33
Carcinoma	8	22	30
Fatty metamorphosis	3	14	17
Acute hepatitis	0	9	9
Biliary stasis	0	7	7
Normal liver	2	6	8
Necrosis	1	4	5
Focal fibrosis	0	3	3
Hemochromatosis	0	2	2
Acute cholangitis	0	2	2
Chronic passive congestion	0	1	1
Hemosiderosis	1	0	1
Amyloidosis	1	0	1
Unsatisfactory	10	9	19

The autopsied cases (table 3) afford an opportunity to check the accuracy of the biopsy diagnoses. In the early period from 1939 to 1943, four diagnoses may be considered to be correct, whereas in two cases the lesion was missed. A case of carcinoma of the esophagus metastatic to the liver in which only blood was obtained by biopsy must be considered an error as must the case of bile duct carcinoma which was called

well differentiated acini. The diagnosis of normal glycogen storage was probably correct but was not subject to check at autopsy because of postmortem tissue

TABLE 3  
COMPARISON OF BIOPSY AND AUTOPSY DIAGNOSIS  
FOR PERIODS 1939-1943 AND 1943-1947  
Diagnoses 1939-1943

Biopsy	Autopsy
1. Blood (2)	Metastatic carcinoma (esophagus)
2. Tumor	Primary carcinoma
3. Normal liver	Focal fibrosis
4. Metastatic carcinoma	Metastatic carcinoma (bronchus)
5. Glandular acini	Bile duct carcinoma
6. Carcinoma	Metastatic carcinoma (trachea)
7. Cirrhosis	Cirrhosis
8. Normal glycogen	Fatty metamorphosis
1943-1947	
1. Hemosiderosis	Hemochromatosis
2. Metastatic carcinoma	Metastatic carcinoma (pancreas)
3. Carcinoma	Metastatic carcinoma (bronchus)
4. Normal liver	Passive hyperemia
5. Cirrhosis	Carcinoma; cirrhosis
6. Cirrhosis	Cirrhosis
7. Cirrhosis	Cirrhosis
8. Metastatic carcinoma	Metastatic carcinoma (esophagus)
9. Cirrhosis	Cirrhosis
10. Carcinoma	Primary carcinoma (liver)
11. Cirrhosis	Cirrhosis
acute hepatitis	subacute hepatitis
12. Obstructive jaundice	Lymphosarcoma with obstruction (stomach)
13. Metastatic carcinoma	Metastatic carcinoma (from colon)
14. Metastatic carcinoma	Metastatic carcinoma (from colon)
15. Cirrhosis	Cirrhosis

changes. During the later period 12 of the 15 diagnoses may be considered correct, but in one, a case of carcinoma (probably primary) of the liver, the diagnosis was missed although the accompanying cirrhosis was correctly diagnosed. The case of passive hyperemia diagnosed at autopsy probably was not present when the biopsy was taken but this cannot be proved. The diagnoses of hemosiderosis and slight chronic periportal hepatitis are not altogether satisfactory in the case of hemo-

chromatosis, though they are consistent.

To assess the clinical value of these biopsies is difficult but it is felt that if the biopsies established a primary diagnosis or confirmed a clinical impression, they were helpful. If they were not in agreement with the general clinical picture but could not establish a diagnosis or were unsatisfactory they were considered not helpful. In the later group it is seen that 91.5 per cent of the biopsies were successful and of these 85 per cent were clinically helpful in contrast to the earlier group.

From experiences with this series of cases it is felt that a biopsy specimen should be obtained in any case of hepatomegaly in which the etiology is unknown. Biopsies have proved particularly useful in following the progress of cirrhosis and in the evaluation of treatment of these and other chronic forms of hepatic disease. Investigation of serial changes in epidemic and toxic hepatitis has been materially advanced by needle biopsy. Further application in these fields is to be expected. In addition the study of living tissue obtained by human liver biopsy may aid in elucidating the normal physiologic function of the liver and its operations in metabolic disease. The use of the Warburg technic with these bits of tissue is under consideration at present.

Generally, it is felt that only easily palpable livers should be needled and that when a biopsy is needed in cases in which the liver is not palpable, either direct biopsy through a small surgical incision or visualization with a peritoneoscope and needle biopsy under guidance should be done. The intercostal approach is not recommended because of danger of tearing the liver should the patient inadvertently breathe while the needle is in the liver and held rigidly between the ribs. Acutely ill patients cannot cooperate in the performance of this procedure and transfixion of the pleural space always carries a hazard of empyema, traumatic pneumothorax or hemothorax or air embolism.

The use of peritoneoscopy in every case is not recommended because it requires ex-

pert training and an expensive instrument and is consequently not widely available. In many cases the liver cannot be visualized because of omental adhesions and the risk is slightly increased. However, in special cases in which a nodule is to be transfixed under vision or the liver cannot be palpated the procedure may be justified.

The two needles in current use each have their advantages. The Silverman instrument is a little easier to handle and gives positive results in a slightly greater percentage of cases; however, the specimens are usually macerated and cellular detail is distorted. The Roth-Turkel needle is larger, yields larger specimens and produces little or no distortion of tissue; however, it is a little more difficult to handle. In some instances it may be impossible to get a specimen with this needle.

It is to be remembered that the tissue obtained is only a small part of a large organ and, although perfectly representative of more diffuse pathologic change, the histologic findings are always to be interpreted with caution. The focal lesions are frequently missed so that a negative result of biopsy does not rule out the presence of tumor, infarction or other localized lesions.

#### SUMMARY

Needle biopsy of the liver has now been done on 128 patients with one serious complication and no deaths. Biopsies have been useful in making diagnoses as well as in following the progress of patients with hepatic disease.

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## THE ETIOLOGY OF PEPTIC ULCER\*

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NEW ORLEANS

### INTRODUCTION

Peptic ulcer is defined in Dorland's American Illustrated Medical Dictionary as "an ulcer seated on the mucous membrane of the stomach or duodenum, caused by the action of the acid gastric juice." In addition "peptic" ulcers occur in Meckel's diverticuli containing functional gastric mucosa, and on the jejunal side of gastro-jejunosomy. Ever since the days of the early nineteenth century, when widespread interest in peptic ulcer really began to manifest itself, numerous theories of etiology have been evolved. As early as 1829 Cruveilhier<sup>13</sup> concluded that gastritis was the predisposing factor in peptic ulcer and recognized that digestion by the acid gastric juice was the mechanism by which the actual dissolution of tissue resistance was effected. In 1848 Rokitanski<sup>35</sup> stated that the lowering of the tissue resistance to acid digestion was probably due to ischemia resulting from organic or functional closure of the blood vessels supplying the mucous membrane of the area involved. In 1852 Gunzberg<sup>22</sup> recognized the erosive effect of gastric juice on the mucous membrane of

the stomach, and in 1853 Virchow<sup>41</sup> restated the opinion of Rokitanski. While an enormous amount of experimental work has been done, and in spite of the fact that we have gained much valuable information of the physiology and pathology of the stomach and duodenum, no one theory has been proposed which will explain all the facts we know about peptic ulcer. If there is ever to be a completely acceptable theory of peptic ulcer, according to Cook and Fuller<sup>12</sup> it must explain the following facts:

1. Location of ulceration in the stomach and duodenum.

2. Rare occurrence of ulcers at the pyloric sphincter.

3. Rare occurrence of ulcers outside the ulcer-bearing area of the stomach and duodenum.

4. Size and shape of ulcers.

5. The occurrence of acute and chronic ulcers.

6. The occurrence of kissing ulcers and saddle ulcers.

7. The age incidence.

8. The sex incidence.

9. The occupational incidence.

10. The presence of pain as a symptom.

11. The disappearance of pain on taking food, and the reappearance of pain when the stomach is about three-fourths empty.

12. The mechanism of effectiveness of medical treatment.

13. The mechanism of effectiveness of surgical treatment.

14. The comparative absence of ulcers in such animals as dogs, swine, and cats.

It will not be attempted in this paper to present a theory which will fulfill all the requirements of these postulates, for no such theory has yet been devised. Nor is it likely that any single, all-embracing theory will be forthcoming, since the etiology probably varies in the different types of ulcer. However, the final mechanism in the production of all gastro-duodenal ulcers is probably the same, that is, digestion of the mucosa by the acid gastric juice. Just what are the predisposing factors making possible this digestion, and why does it not occur

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in all individuals with free hydrochloric acid in the gastric juice, are factors which will be discussed. We shall not be greatly concerned in this discussion with Curling's ulcers, or those produced by unphysiologic means. We shall deal chiefly with the gastro-duodenal ulcer for which there is no obvious etiology, and cite the results of some of the unphysiologic experiments to uphold or disprove ideas which have been derived from clinical experience and from experiments with normal individuals and with ulcer patients.

#### THE PSYCHOSOMATIC AND CONSTITUTIONAL ASPECT OF PEPTIC ULCER

The importance of acid digestion in the production of peptic ulcer has long been recognized, and it has been adequately demonstrated that most ulcer patients have hyperchlorhydria. However, the factors leading to the excess secretion by the gastric mucosa are not well known, nor is it known why the gastric or duodenal mucosa of the ulcer patient is sometimes digested by a gastric juice which contains no more acid than is seen in some normal individuals. Is it not reasonable to assume that there is something inherent in the constitution-personality pattern of the individual which causes gastric hypersecretion and/or decreased resistance of the gastrointestinal mucosa to digestion. In seeking the answer to this long unsolved question, Wolf, Stewart, and Wolff<sup>45</sup> had the unique opportunity to study a modern Alexis St. Martin, including a careful correlation of emotional status with gastric function. This subject was 56 years of age and had been feeding himself through a 3.5 cm. surgical gastrostomy since the accidental occlusion of his esophagus at the age of nine years. According to these authors the man was in excellent health and rarely had stomach trouble. "He is shy, proud, sensitive, stubborn, and slightly suspicious. He is fun loving, but very conscientious." He had a collar of gastric mucosa protruding on the abdominal wall, and estimates of vascular change were made by comparing the color of the gastric mucosa to a standard scale. These estimates were checked by a blood

flow recording device. Standard analyses of the gastric content were made from aspirated specimens, and a careful note of the mood, content of thought, and preoccupations was made. No artificial situations were created for purposes of this study, and only situations naturally occurring in the life of this individual were analyzed. The following facts were noted and conclusions reached:

1. Acid in small amount was secreted continuously.
2. Spontaneous increase in acid production was accompanied by blushing of the mucous membrane and an increase in the motility of the stomach.
3. Fear and sadness, which occurred infrequently, were accompanied by a decrease in acid and a decrease in stomach contractions.
4. Conflict involving anxiety, hostility, and resentment were accompanied by increased acid and motility, and by hyperemia. These responses were much more frequent than fear and sadness.
5. Intense, sustained anxiety, hostility, and resentment were accompanied by prolonged engorgement, hypermotility, and increased secretion. Erosion and hemorrhages appeared spontaneously or were elicited by slight trauma.
6. The stimulation of an erosion by gastric juice caused an increase in acid and more general engorgement.
7. The lining of the stomach was protected by mucous. There is no mucous in the duodenum.
8. It is likely that this mechanism is present in the average ulcer patient.

Since it is now believed that there is a close connection between the psychic state of the individual and his gastric function, and since this connection is probably mediated by peripheral nerves, it is important to understand the innervation of the stomach. The following explanation is given by Best.<sup>7</sup> The abdominal viscera are under the control of the sympathetic and the parasympathetic nervous systems, which are more or less antagonistic, and which are



more or less in balance. The action of the autonomic nervous system is influenced by many intrinsic and many extrinsic factors. Stimulation above a certain level, which varies for each individual, and which Best calls the "threshold of endurance" results in an upset of balance, and in some cases, there is an increase in parasympathetic outflow, and in some cases a decrease in sympathetic activity. The upper viscera get their parasympathetic supply from the cranial outflow (vagus nerve) which arises from vegetative centers (involuntary) which are connected with the cortical centers (voluntary). The colon and lower viscera are supplied by the sacral outflow. Vagal stimulation results in hypertonicity or spasm of the pyloric sphincter, hypermotility of the entire gastrointestinal tract, and prolonged secretion of hyperacid gastric juices. Secretion of the protective mucous is first stimulated, and then inhibited. Because of the pyloric spasm the stomach has atony and the gastric content is retained. In addition, regurgitation into the stomach of the alkaline intestinal juices and bile is interfered with, and a further obstacle to neutralization of the acid gastric juice is imposed. Furthermore, the spasm of the pyloric sphincter interferes with the blood supply of the mucous membrane, and resistance is further decreased. This pathologic physiology may occur in any given individual intermittently or constantly for varying lengths of time. Almost every feature of this functional state predisposes to digestion of the mucous membrane, and according to Best any given person has only a limited capacity for endurance of the state. The non-acid secreting portion of the stomach and the first portion of the duodenum, which are most susceptible to acid digestion, are naturally the first to succumb.

The next problem that arises is what makes some individuals vagotonic, or what gives them a low threshold to stimuli which produce a parasympathetic overflow, or what gives them a lowered endurance to the state of parasympathetic overflow. At this point we leave the field which is in the realm of anatomy and physiology and enter

the fields of psychobiology, psychiatry, and psychoanalysis. The psychoanalytic school, according to Lapinsohn<sup>28</sup> describes the following as a typical pathogenesis of the personality pattern characteristic of the ulcer patient. They state that certain unhappy experiences interfere with normal psychosexual development, and the individual fails to mature emotionally. This failure to mature increases passive wishing, as passivity is correlated with earlier stages of psychosexual development. If such an ego is thwarted aggressively, it reacts by feelings of inferiority and guilt. However, the whole process is concealed under a flood of overcompensation, manifested by an independent, responsible attitude in adult life. This regression to passivity causes a fusion of the oral and the passive attitudes, that is, wishes to be loved, and wishes to be fed. The individual thus regresses emotionally to the infantile, passive state where being fed and being loved were characteristic of this emotional stage. The wish for care is repressed, but is easily converted to a desire to be nourished. Thus, there is initiated a continuous, unconscious, psychic stimulus which provokes vascular, secretory, and motor responses in the gastrointestinal tract until it behaves as if it were taking food. The constant hypersecretion is not counteracted by its natural antagonist, food, and thus it has the opportunity to digest the mucous membrane. Or, stated another way, emotional conflict leads to functional change in the organ affected, which results with time in organic change.

Katz<sup>26</sup> states that ulcer is a disease of civilization. It is absent in parts of the world where stress and tension are minimal. He characterizes the ulcer patient as a hypersensitive, hyperirritable, hyperactive, individualist who has a great deal of drive and who is very meticulous. Distress often begins in the adolescent period when profound physiological and emotional changes occur. Katz states that they have "vague 'stomach pains,' diarrhea, severe constipation, and flatulence." The x-ray shows little at this time. Bokus calls these conditions "pseudo-ulcer," or "pyloro-duodenal irrita-

bility," and says that they are an intermediate stage of ulcer.

In a psychoanalytic examination of 33 young adult males with gastric or duodenal ulcer, Winkelstein<sup>44</sup> and Rothschild<sup>36</sup> found a highly characteristic psychic background. According to these workers, the ulcer patient suffers from chronic frustration, and inward direction of repressed, strong, emotional stimuli with prominent sadistic and masochistic features. They state that the inward tension or drive bears a close relationship to the incidence and recurrence of peptic ulcer, and that they believe that peptic ulcer is definitely a psychosomatic disease.

One study by Bolen<sup>8</sup> in connection with the emotional factors in peptic ulcer is very instructive. He took 40 patients with chronic ulcer of long duration and 40 patients of the nervous type with ulcer and with symptoms that disappeared when emotional tension was discovered and eradicated. He determined the free and total acid after a 12 hour period of fasting, and used samples aspirated every 15 minutes for one hour. He considered 20-40° free HCl normal, 40-60° moderately high, and over 60° markedly high. All these patients had x-ray evidence of ulcer, and they were studied only when they exhibited symptoms. The majority of patients in both groups had more than 40° free acid. The patients in group I, in whom no emotional factors were elicited, were kept on a modified Sippy diet, and they remained symptom free as long as they adhered to it. The patients in group II, in whom emotional factors were elicited, had the same symptoms as those in group I, but the severity of their symptoms varied proportionately to the amount of emotional stress. Upon removal of the specific disturbance, the symptoms disappeared. There was a definite decrease in free acid and in total acid when the symptoms ceased. The obvious conclusion to be reached from the results of this experiment is that the gastrointestinal system is closely bound up with the psyche by means of the autonomic sys-

tem, and that ulcer symptoms are relieved when emotional tension is relieved.

In addition to there being a personality pattern which is characteristic of ulcer patients, there is a constitutional or structural pattern as well. Lapinsohn<sup>28</sup> quoting Sheldon says that the ulcer patient usually has a slender, moderately large trunk with a lightly built frame. The shoulders are broader than the waist, and the chest is somewhat larger than the abdomen. The patient is high to tall. He then introduces the terms "gynandromorphy" and "andromorphy." These refer to the bisexuality of a physique, the occurrence of the secondary sex characteristics of the opposite sex. The characteristics of gynandromorphy according to Sheldon are the following:

1. Widened hips
2. Broad pelvis, fine form
3. Female hair distribution
4. Fatty simulation of mammary development
5. Small and underdeveloped arms
6. Soft and velvety skin
7. Well developed outer curve of the leg
8. Small facial features with softened relief
9. An intrusion of softness
10. Long eyelashes

The gynandromorphic index, or the number of these listed features occurring in the male patient, is low in the gastric ulcer patient, but very high in the duodenal ulcer patient.

Lapinsohn further states that the electroencephalogram of the ulcer patient shows alpha waves three and one-half times as frequent as in the normal individual. He states that this is compatible with the passive, receptive type which these people actually are under their front of aggression and independence. In addition they characteristically have an electrocardiogram which shows a slow sinus arrhythmia, and a prolonged P-R interval, also indicating vagotonus.

#### GASTRIC ACIDITY IN ULCER PATIENTS AND IN NORMAL INDIVIDUALS

In spite of the fact that much has been conjectured about gastric acidity in ulcer



patients, we still have very little actual information on the subject. Most of the information obtained has been derived from aspirated gastric content from fasting individuals or from individuals after administration of some kind of "test meal." Most of the test meals are designed to stimulate one fraction or another in the gastric content, but few if any are physiological. Information on the fluctuations in the gastric acidity over 24 hours of normal activity in the normal individual or in the ulcer patient eating regular meals is totally lacking. The reasons for this are mostly technical ones. It is virtually impossible to keep a stomach tube in a patient for any prolonged period. Also it is very difficult or even impossible to feed the subject normal meals and have them elicit the usual gastric response, and at the same time evacuate the stomach in order to make the necessary analyses. In addition, the analysis of gastric content containing food remains is totally unsatisfactory.

However, the problem has been approached in various ways. One very enlightening study was done by Sandweiss, Sugarman, Podolsky, and Friedman.<sup>37</sup> They report a study on the nocturnal gastric secretion in 38 normal and 29 duodenal ulcer patients. They conducted their study at night because the gastric juice is less contaminated at that time, and because they were interested in that seven or eight hour period when the stomach is empty and the gastric secretion is not neutralized by extrinsic agents. For purposes of this study they fed their subjects a fairly normal meal at 6:00 p. m. It consisted of 45.1 gm. protein, 42.7 gm. fat, and 109.8 gm. carbohydrate, totaling 992 calories. They obtained the following results:

1. There is a much lower titratable acid after the meal than before it, presumably because of the absorption and dilution of acid by the meal. Only after 9:00 p. m. did the concentration of acid begin to rise.

2. Curves of acid concentration in the normal individual and in the ulcer patient are the same until 12:00 p. m. However, the

acid concentration goes higher in the normal individual after this time.

3. Fifty-three per cent of normal males and 24 per cent of ulcer patients had over 70° acid during the night. This is considered abnormal.

4. The authors obtained a consistently greater volume of gastric juice in the ulcer patient. However, this is true only if aspirations are performed every hour or once during the eight hour period. If continuous aspiration is employed, the volumes obtained are not significantly different. The inference is that the ulcer patient does not hypersecrete, but does have a certain degree of gastric retention.

Another interesting and illuminating study in this problem of gastric secretion was done by Berk, Rehfuess, and Thomas.<sup>6</sup> They selected 23 active duodenal ulcer patients at random, all having x-ray evidence of the lesion, and a group of normal individuals with no abdominal complaint. The subjects swallowed a double lumen tube before breakfast, after having fasting for 12 hours. The tip of the tube was shown to be in the duodenum by fluoroscopic and x-ray methods, and samples were drawn simultaneously from the stomach and duodenum every 10 minutes for half an hour. The pH of each sample was determined electrically, and the free and total acid was titrated using the standard indicators. In addition, the "excess neutralizing ability", or "the amount of N/10 HCl necessary to bring about a positive colorimetric reaction for free acid" was obtained on the samples. The average pH in the stomach of the fasting ulcer patient was 1.65 compared to 3.51 for the normals. In the duodenal samples (fasting) the average pH for ulcer patients was 3.69 compared to 5.60 for the normals. There was a consistent overall increase in the acid of the ulcer patient but a consistently greater difference in the pH of the gastric and duodenal samples than in the normal subject. The duodenal ulcer patient showed less acidity with each succeeding aspiration, and fluctuation in the reaction of the contents of the duodenum was more pronounced in

ulcer patient, but not as great after fasting as during digestion.

The average excess neutralizing ability of the duodenal contents was  $11^{\circ}$  which is less than that which is found in fasting normals,  $17^{\circ}$ , or in the patient with ulcer after the Ewald test meal,  $14^{\circ}$ . Thirty-seven and one-half per cent of ulcer patients failed to show excess neutralizing ability whereas only fourteen and one-half per cent of normal individuals failed to show it. Of the ulcer patients who had taken the Ewald meal, forty-one and three tenths per cent failed to show excess neutralizing ability. These authors state that the values obtained in their determinations may not be quantitatively correct, but that they serve as good comparative measures. To summarize, they found that gastric acidity is higher in the duodenal ulcer patient than in normal individuals; fasting gastric acidity in these patients is almost the same as that after the Ewald test meal; the contents of the duodenum are not only more acid in the fasting patient than in the normal, but that duodenal neutralizing ability is overcome for a longer period; the neutralizing ability of the duodenum is defective in the duodenal ulcer patient, and it is almost as good fasting as during a meal. This latter finding may represent increased neutralizing ability in the fasting state or impaired neutralizing ability after eating.

#### EVIDENCE FOR THE ACID DIGESTION THEORY OF ULCER PRODUCTION

There can no longer be any doubt that the actual dissolution of the gastro-intestinal mucosa in the production of peptic ulcer is brought about by the action of the acid gastric juice. This can be shown in two principle ways. As has been demonstrated many times, we can produce peptic ulcer either by stimulating excessive acid gastric secretion or by removing the physiological antagonists of those secretions. Koellinker and Miller, quoted by Driver and Carmichael,<sup>16</sup> in 1851 were the first to observe that dogs and other animals with biliary fistula frequently develop gastric and duodenal ulcers. In 1932, Bollman and Mann found that ligation of the common

duct produced ulcers in sixty per cent of dogs, and in 1935 Blanck found that ulcers caused by loss of bile in dogs could be prevented by feeding bile by mouth. In perfusion experiments by Driver and Carmichael, using isolated loops of gut in anesthetized dogs, and exposing them to acid-pepsin mixtures both with and without bile salts, they obtain some very striking results. They found that the presence of bile salts in the perfusion material greatly inhibited the peptic digestion of the intestinal wall at a pH of 1.25, and prevented perforation of a margin of 138 minutes with bile as contrasted with 82 minutes when no bile was used.

The following experimental work cited by Code<sup>11</sup> also points unquestionably to the production of peptic ulcer by the acid gastric juice. Abolition of pancreatic secretion by ligation of the ducts resulted in six duodenal ulcers out of sixty-one dogs, in experiments by Ivy and Fauley. Loss of the duodenal secretion by removal of the duodenum and replacing it with jejunum, into which the bile and the pancreatic ducts have been transplanted resulted in ulcer in twenty per cent of the dogs operated upon by Mann and Kawamura and Mann and Williamson. By ligating the common bile duct, Mann and Bollman secured 73 per cent peptic ulcers in their series. By creating the loss of pancreatic juice, succus entericus, and bile, by means of duodenal drainage, Mann and Williamson secured 88 and 95 per cent ulcers in two of their series, and Morton, and Fauley and Ivy secured 100 per cent ulcers in similar experiments.

In addition to producing ulcer by removal of the physiological antagonists of gastric secretion, we can also produce this lesion by stimulating excess secretion of hydrochloric acid and the ferments which usually accompany it. We can not only stimulate excess gastric secretion, but we can simulate and exaggerate two of the important phases of digestion. We can simulate the psychic and oral phase of digestion by ham feeding as was done by Silverman (quoted by Code<sup>11</sup>). He did esophagostomies on 23 healthy adult dogs and fed them orally three



times a day between the three meals which were fed by a surgical gastrostomy. Eighteen of the dogs developed ulcer in 14 to 17 days. Their gastrostomy meals consisted of meat, bouillon, and bread, which they received alternately with the sham meals. Here we see duplicated almost perfectly the constant gastric secretion of nervous origin as is postulated by the psychiatrist in cases of chronic anxiety. Also we see well demonstrated the results of the action of the powerful acid gastric juice, not neutralized by one of its most important antagonists—food.

On the other hand we can use histamine, the gastric hormone (?), to simulate a continued chemical phase of digestion. The method utilizing histamine in beeswax to produce peptic ulcer was developed by Varro and Code in 1940 (quoted by Code<sup>11</sup>). They found that a prolonged gastric hypersecretion was produced by histamine used in this manner, and that they could obtain an equivalent of one to two liters of N/10 HCl in 24 hours with one injection in dogs with gastric pouches, compared to a four hour period of stimulation produced by injecting aqueous histamine, which resulted in only about 100 c.c. of secretion. Using this important new experimental method for ulcer production, they obtained twelve ulcers in 13 dogs within a period of 30 days, using daily injections. In another series of experiments with gastrectomized dogs, no ulcers were obtained. Obviously the mechanism for ulcer production here is gastric hypersecretion.

#### THE RELATION OF Pepsin TO PEPTIC ULCER, AND THE ROLE OF MUCOUS IN PROTECTING THE MUCOUS MEMBRANE FROM PEPTIC DIGESTION

It was observed by Komarov<sup>27</sup> that dogs with Pavlov type gastric pouches, which secrete a strong acid and a high concentration of pepsin can live for years, even though as much as 200 c.c. of this powerful mixture would accumulate in 24 hours, and even though it would not be aspirated more than once a day. These animals do not develop peptic ulcers. However, if the juice from one of these pouches were allowed to come into contact with the animal's skin, a

huge ulcer would develop in only a few hours. No material was present in the pouch that was not present on the skin except mucous. He further observed that dogs with the Heidenhain type of pouch, which secretes much acid but very little pepsin, do not develop ulcers if the juice from their pouch comes into contact with their skin. This led him to pursue two ideas—first, that pepsin is necessary for acid digestion of the gastrointestinal mucous membrane; and second, that there is something in or on the lining of the living stomach that protects it from digestion by its own secretion.

In following up the first idea Komarov quotes a very important piece of experimental work by Schiffrin, in which time the latter perfused isolated loops of cat intestine with HCl at a pH of 1.2, both with and without pepsin added to the mixture. In using the pepsin containing mixture, he consistently got bleeding, ulceration, and frequent perforation. In using plain HCl solutions for perfusion material, he noted few, if any, harmful effects in the intestinal loops perfused. He found that he did get bleeding and ulceration when using acid alone in perfusion of the stomach or in perfusion of the duodenum through the stomach. However, upon closer examination, he always found pepsin in appreciable quantities in the perfusate. Even here, however, ulcers were produced much quicker if an acid-pepsin mixture were used than if acid alone were used. In further work along this line Schiffrin instilled acid-pepsin mixtures hourly into fasting cats' stomachs for periods of eight hours and found that the cats died in five to eight days with ulceration and hemorrhages. These cats perfused with acid alone survived. Schiffrin concluded that pepsin is necessary for ulcer production.

In pursuing his second idea, Komarov reviewed the literature on the chemical and physical properties of gastric mucous and tried to determine its efficacy in neutralizing the acid-pepsin mixture which normally occurs in the gastric secretion. From his studies he concluded that the surface

mucus, which is secreted constantly by the gastric epithelium, is effective in neutralizing or otherwise inactivating gastric juice and in protecting the gastric mucosa by virtue of their properties:

1. Mucus consists largely of a mucoprotein not soluble in dilute HCl. Its viscosity increases with the acidity of the gastric content, and thus it can mechanically prevent contact of the acid-pepsin mixture with the mucous membrane.

2. It can buffer, absorb, and neutralize HCl.

3. It is relatively resistant to digestion. It is digested slowly at 37° C. by acid-pepsin mixtures, but after dissolving it forms an acid-insoluble precipitate which is more resistant to digestion than the original mucus.

Komarov presents some evidence from the literature of a postulated ferment "anti-pepsin." Many men have claimed to have isolated it, but all of them seem to disagree upon what its physical properties are. Komarov agrees with Lagenskiöld that the effects noted can be explained on the presence of albumoses and peptoses, and in some cases even to inorganic salts which may have contaminated the supposedly "pure" substances isolated.

#### ENTEROGASTRONE AND UROGASTRONE

Besides the protection of the gastrointestinal mucous membrane by food, regurgitation of the alkaline intestinal juices, mucus, and the possible "anti-pepsins", another mechanism of possibly great importance has been discovered. It has long been known that fat and sugar inhibit gastric secretion and motility, and induce a temporary gastric retention. However, it has only recently been discovered that the mechanism for this action is the production of a hormone called enterogastrone from the mucosa of the upper intestinal tract. According to Ivy<sup>25</sup> it can be obtained as an extract of the upper intestinal tract and is effective even when given parenterally. Fractions can be obtained which will inhibit either the acid secretion or the motility of the stomach independently of the other function, so "enterogastrone" is

probably composed of more than one substance. Also it has been discovered that the urine of dogs and man contains substances which inhibit gastric secretion and motility. This, of course, suggested the idea that the urinary substances may represent the excreted form of enterogastrone. The urinary form has been called "urogastrone."

Many interesting facts have been discovered about these two substances and their bearing on gastro-intestinal physiology and pathology. It has been found that an increase or decrease in the fat content of the diet of man or dog will increase the amount of urogastrone in the urine of man or dog. Also it is believed that the peptic ulcer patient excreted less urogastrone than the normal individual. When the gastro-intestinal tract of the dog is removed, the urogastrone excretion diminishes greatly, but is not entirely abolished. The remaining anti-ulcer substance may be non-specific, however. It is also known that pepsin will inactivate enterogastrone but does not affect urogastrone. Urogastrone has been tried in the treatment of the ulcer patient, but its use had to be discontinued because it caused a local swelling at the site of injection several hours later.

Some experimental work with enterogastrone on dogs has been done and it gives very promising results as a possible cure for ulcer patients. In dogs with the Mann-Williamson operation, 98 per cent die within 1 to 9 months with ulceration of the stomach or duodenum. However, in 33 dogs with this operation performed, in which enterogastrone was administered, only 25 per cent developed ulcer. Ivy states that these dogs probably became refractory to the material. After preventing ulcer in these dogs for one year, the enterogastrone was discontinued. In 11 dogs no ulcer developed in one year with no treatment. Seven out of eleven were alive one and one-half to two years after cessation of treatment.

The actual mechanism for the protection of the gastrointestinal mucosa by this intestinal extract is now known. However there are four proposed mechanisms which



may be of importance. It may cause a decrease in the production of acid, a decrease in production of pepsin, an increase in resistance of the gastrointestinal mucosa to the acid-pepsin mixture, or may work by some combination of these mechanisms. Ivy has actually observed a lessened tendency to prolonged acid secretory response after a meal. He has likewise noted a decrease in the production of pepsin, though its production is not abolished. As to the increase in resistance of the mucous membrane, we can only speculate about for the present, at least, since we have no adequate method of objectively measuring tissue resistance. Enterogastrone has been given to fifteen ulcer patients who have had two or more recurrences of symptoms annually, and palliative results have been obtained. However, the series is not large enough to be of statistical significance yet.

#### THE ROLE OF THE VAGUS NERVE IN PEPTIC ULCER

In view of the importance which is now being attached to the psychosomatic etiology of peptic ulcer and to neurogenic causes, both of which presuppose that the vagus is a link in the pathway from the cerebrum to the stomach, it becomes important to know how much significance to attach to this nerve in normal stomach secretion and in the secretion of the ulcer patients. It likewise is important to know whether individuals with bilateral vagotomy could develop peptic ulcer, and whether vagotomy would be beneficial in the treatment of ulcer cases. Unfortunately, all the answers are not known. However, some valuable steps toward answering them have been taken. Winkelstein<sup>44</sup> has made many valuable observations. Using special means, consisting of chewing an orange to stimulate the nervous phase of digestion, and injecting beef bouillon into the stomach of the individual without his knowledge in order to stimulate the chemical phase, he found that the nervous phase is hyperactive in ulcer patients and the chemical phase is normal. Using histamine, which closely stimulates the action of the gastric hormone, he obtained only a moderately high response in the ulcer upon using fifteen units of insulin intra-

patient as compared to normal. However, venously and producing a marked hypoglycemia, which is a powerful stimulus to the vagal nucleus, he found that the ulcer patient responds with a very high gastric secretion as compared to normal individuals receiving the same test. Furthermore, in his studies on nocturnal gastric secretion he found that the ulcer patient has a higher acidity and a large volume of secretion during the night whereas the normal individual has little or no secretion. He believes that nocturnal secretion is of vagal origin. Also after a partial gastrectomy many of the patients continue to secrete free hydrochloric acid. Winkelstein reasons that since the source of the gastric hormone is gone, the acid must be of vagal origin. Furthermore, it has been demonstrated repeatedly that electrical stimulation of small areas of the hypothalamus and of the vagus can produce ulcers in the stomach and duodenum of animals.

Dragstedt<sup>15</sup> has also done some very important experimental work in this field. He found that in dogs in which the stomach had been isolated from the rest of the gastrointestinal tract and in which the gastric secretion was recovered by a cannula, the volume of secretion was reduced by vagotomy from 1100 c.c. a day to 410 c.c. a day, and the acid was reduced from .35-.42 per cent before the operation to .11-.32 per cent afterward. He too believes that the hypersecretion in ulcer patients is neurogenic, and that the vagus is the pathway for the stimulus.

As to results in the ulcer patient receiving vagotomy, the preliminary reports are very promising. In 1945 Dragstedt reported on 39 cases on which he had performed the operation for peptic ulcer. Thirty-two received a supra-diaphragmatic vagotomy bilaterally, and the proximal ends of the severed nerves were sewn into the pleural cavity. Seven patients received an infra-diaphragmatic vagotomy because of a high grade stenosis necessitating gastroenterostomy or resection. In the last 21 patients operated upon, a positive response to the insulin test was elicited in all before op-

eration. Only one doubtful reaction was observed in the group after operation. The rest of the patients gave an entirely normal response. Of the first patients operated upon, all but one have obtained striking and persistent relief from symptoms two and one-half years after the operation. They live on unrestricted diets and without medication.

Winkelstein<sup>44</sup> quoting Berg's results in 34 vagotomies states that there was a post-operative achlorhydria in 26 cases, and that 31 have remained well four to nine years after operation. He points out, however, that vagotomy should not be done in cases of pyloric obstruction with atony, since vagotomy decreases the tone and peristalsis of the stomach. He further cautions that vagotomy should only be done after subtotal gastrectomy, since atony of the entire stomach produces distressing symptoms.

In 25 cases of transthoracic vagotomy reported by Grimson, Taylor and associates<sup>21</sup> they claim results comparable to those of Dragstedt, and agree with him on the rationale of doing the operation for peptic ulcer. They too point out that vagotomy must be combined with pyloroplasty or gastro-jejunostomy in cases of pyloric obstruction for best results.

As to what objective benefits the patients may derive from vagotomy, we have this much information from the authors who have performed the operation. Grimson, Taylor and associates say that there is a temporary but definite and significant decrease in the response to histamine post-operatively. There is a permanent decrease in the response of insulin, and besides a decrease in the volume of gastric secretion and the acidity of the secretion, there is a prominent and constant decrease in the motility of the stomach. Dragstedt agrees that postoperative secretory response to insulin is abolished, and that there is a marked decrease in motility of the stomach. However, he points out that intestinal peristalsis is increased, and that some of the patients have even been relieved of constipation by the operation. He found, as did Barnofski, Friesen, et al.<sup>4</sup> that vagotomy does not re-

duce the response of the stomach to histamine. The latter authors found that bilateral vagotomy does not protect dogs from ulcers produced by daily injections of histamine in beeswax.

#### SOME SPECIAL TYPES OF PEPTIC ULCER

There are undoubtedly many factors in the etiology and pathogenesis of peptic ulcer which we have not touched on. Indeed many special types of "peptic" ulcer exist which are produced rather constantly under a given set of conditions or which have a plausible connection with some special insult to the body. We shall mention only a few of these.

One such special type of ulcer is Curling's ulcer. It has long been known that the ulcer can be reproduced in dogs, if sufficiently large areas of skin are burned away. The exact mechanism for production of this type of peptic ulcer is not known. Hartman<sup>23</sup> suggests that one or more of these four mechanisms is at work and gives some experimental evidence in favor of each:

1. Hyperacidity of gastric secretion.
2. Action of a burn toxin.
3. High blood concentration resulting in stasis and hemorrhage.
4. Sepsis, causing petechiae in the gastrointestinal mucosa and leading to ulcer formation.

He points out that in a series of dogs in which he produced second and third degree burns experimentally, he could reduce the incidence of Curling's ulcer from 63.3 per cent to 6.6 per cent by changing the therapy from a vaseline dressing to a tannic acid dressing. The significance of this finding in the etiology of Curling's ulcer is not known.

Another type of ulcer which has had much publicity, but which has not been so well established by objective experimentation and reasoning, is the traumatic ulcer. Fowler<sup>19</sup> believes that there is such an etiology for peptic ulcer, and states that he has satisfied himself of the authenticity of 35 cases, collected from the literature from 1840 to 1941, and of 42 cases out of 7050 reviewed from the literature of 1941 to 1943. The absolute criteria which have



been set up for determining a traumatic ulcer are quite academic and very difficult, if not impossible, to apply to the actual case. However, using the author's modification of criteria set up by Lenninger and Molenius, he states that approximately 0.6 per cent of the cases he reviewed were of traumatic origin.

The "neurogenic" ulcer is one which has been recognized and accepted for many years. In a lengthy review of the subject, Balo<sup>3</sup> gives the following historical account of neurogenic ulcer. In 1841 Rokitsanski described a type of stomach ulcer connected with intracranial damage of the newborn and another found in children and in adults as a result of pathology in the brain and meninges. In 1845 Schiff found that unilateral damage to the optic thalamus and peduncle may cause softening and even perforation of the stomach. He also found that this effect was abolished by severing the vagus. Westphal and Underhill produced erosions of the rabbit stomach by stimulating the vagus with pylocarpine. In 1932 Cushing observed peptic ulcer caused by removal of a brain tumor. In view of these facts we might expect to see a high incidence of intracranial damage in ulcer patients who come to autopsy. However, such is not the case. Balo quotes Greiss as finding central nervous system changes in only 5 per cent of 138 ulcer cases, and Vonerahé as finding only 21.6 per cent of brain disease in his series of ulcer cases. Balo himself found hemorrhages in the brain or meninges of 32 per cent of his ulcer cases at autopsy. However, only 12 per cent of the cases showed gross hemorrhage.

One other syndrome is of interest to us at this point. It has been noted often in practice that fracture of a long bone is followed by hematemesis. Wangensteen<sup>43</sup> was able to produce peptic ulcer in 53 per cent of dogs by drilling a hole in both sides of the humerus (piercing both cortices) or by drilling a hole followed by curettage, or by fracturing the humerus. The question arises, is the ulcer due to a histamine effect and gastric hypersecretion, or is it due to

fat embolism, or are both factors operating here. It is interesting to note that neither the dog with the experimental fracture nor the patient with the accidental fracture shows hyperacidity except very rarely. To demonstrate or rule out the action of fat embolism in this instance Wangensteen injected intravenously 1.5 c.c. of fat per kilogram body weight into rabbits, simultaneously injecting histamine in beeswax. Almost 100 per cent of these animals developed ulcer, whereas rabbits injected only with histamine in beeswax seldom developed ulcer. The fat does not cause an increase in acidity, so we must presume embolism, ischemia, necrosis, and acid-peptic digestion as the mechanism at work here. Wangensteen points out that it was known as long ago as 1916 (Bissell) that fat emboli are frequently found in the brain and lungs of people dying early after the fracture of a long bone. So the assumption is that fat embolism after bony fracture may cause peptic ulcer.

#### SOME OTHER HYPOTHESES ON PEPTIC ULCER

So many other experimental methods have been devised for the production of peptic ulcer, and so many other theories about the predisposing and precipitating factors of peptic ulcer have been set forth that it is not within the scope of this paper to discuss all of them in detail or even mention each of them. Only a few of the suggestions, theories, and experimental methods which may be of importance will be mentioned. One interesting hypothesis is that proposed by Steven<sup>39</sup> who suggests that peptic ulcer may be due to an increase in the amount of the intrinsic factor of Castle. He points out that pernicious anemia and peptic ulcer occur together only very rarely. However, he gives no experimental evidence for this idea. Barnofsky<sup>5</sup> points out the old idea that peptic ulcer may be based on thrombosis of gastric vessels superimposed upon a previously existing arteriosclerotic process. However, he is quick to point out that peptic ulcer is a disease of young adults, whereas arteriosclerosis is a disease of those past middle age. Walter<sup>42</sup> points out that ulcers occur

more frequently in persons who sit a great deal. He also points out that sitting on the sacrum is a common habit, and that this odd posture pushes the costal arch inward, compressing the lesser curvature of the stomach and the cap of the duodenum, causing ischemia and predisposing to acid digestion of the mucosa. Along this same line Ehrmann<sup>17</sup> recalls that individuals with kyphosis or scoliosis or both in Germany frequently got peptic ulcer during World War I when food was scanty there. He too believed that the stomach and duodenum can be compressed between the vertebra and the costal arch, and that this compression does predispose to peptic ulcer. He also recalled that when food became more plentiful and those peptic ulcer patients accumulated some fat in the peritoneum and in the abdomen, the stomach was cushioned against compression of the bony cage, and the incidence of peptic ulcer declined. Hebel<sup>24</sup> brings up the old question of the bearing of gastric infection and inflammation on peptic ulcer. In 260 stomachs at autopsy, from individuals having no abdominal complaint, he found remarkable change in the gastric mucosa rare under 30 years, and uncommon under 50 years. But in 106 stomachs resected for ulcer, 78 for duodenal ulcer and 15 for gastric ulcer, and 14 for gastric and duodenal ulcer, there was an antral gastritis in all 98 cases in which the antrum was examined. Changes in the body mucosa were rare in the duodenal ulcer cases, and common in the gastric ulcer group. The author believes that this substantiates his idea that antral gastritis precedes and is the anatomic basis for the development of peptic ulcer.

#### A FEW OF THE OTHER EXPERIMENTAL PROCEDURES USED IN THE PRODUCTION OF PEPTIC ULCER

Many experimental procedures have been devised for the production of peptic ulcer in animals. Quite a few of these are so far removed from any conceivable natural or environmental condition that they are indeed difficult to evaluate. However, certain of them demonstrate principles which may operate in the actual patient, and therefore may be of value. Necheles<sup>34</sup> has produced

peptic ulcer in dogs by injecting rather large doses of caffeine in beeswax. He and his associates also showed that 73 per cent of human subjects show a sharp rise in acidity and volume of secretion following two cups of black coffee. They attribute the action of caffeine directly on the parietal cells of the stomach glands. Nedzel<sup>33</sup> has produced peptic ulcers in a large percentage of dogs by injecting them with pitressin intravenously. He attributes the action to a severe vasoconstriction and ischemia which is produced in the stomach wall. Shay and his coworkers<sup>38</sup> have produced peptic ulcer in the rumen of the rat stomach by tying off the pylorus.

#### SUMMARY AND CONCLUSIONS

1. No theory of the etiology of peptic ulcer yet proposed has been able to explain all the facts we know about the condition.
2. According to Wolf, Stewart, and Wolff, from their observations on a gastric fistula subject, intense anxiety, hostility, and resentment are reflected in the stomach by engorgement with blood, hypermotility, and hypersecretion.
3. The stomach and duodenum are under the control of sympathetic and the parasympathetic nervous systems, and the ulcer patient seems to be particularly sensitive to the influence of the parasympathetic system (vagal control).
4. The ulcer patient's personality is characterized by a high degree of individuality, plus hypersensitivity, hyperirritability, and hyperactivity.
5. The ulcer patient who has detectable and removable psychic disturbances has a reduction in gastric acidity when the emotional factors are eliminated.
6. The patient with duodenal ulcer has a high gynandromorphic index, that is, he has many feminine secondary sex characteristics.
7. The nocturnal gastric acidity of the duodenal ulcer patient is no higher than that of the normal individual, but some gastric retention is present in the ulcer patient.
8. Gastric acidity is higher in the duodenal patient than in normal individuals.



Duodenal bulb neutralizing ability is impaired in the duodenal ulcer patient after eating.

9. Peptic ulcer can be produced by operations which divert the physiological antagonists of the gastric secretion, that is, bile, pancreatic juice, and succus entericus, and by stimulating increased gastric secretion using the methods of sham feeding and injections of histamine in beeswax.

10. Pepsin is necessary in the gastric juice for the production of peptic ulcers. Mucus protects the stomach from digestion because of its chemical and physical properties.

11. A fraction of the extract of upper intestinal mucosa, enterogastrone, and a fraction of human and canine urine, urogastrone, decreases the acidity and motility of the stomach, and helps prevent experimental ulcer in the dogs.

12. Vagotomy will prevent the gastric hypersecretion produced by fifteen units of insulin intravenously in the ulcer patient but will not prevent his response to histamine. Vagotomy is of therapeutic value in selected ulcer cases.

13. Peptic ulcer occurs rather frequently in cases of special types of body trauma, such as third degree burns: strong, blunt abdominal trauma; fracture of long bones; and some central nervous system lesions and injuries.

14. Peptic ulcer can be produced in a number of ways experimentally, such as by injecting cincophen, caffeine, pitressin, or by ligating the pylorus in the case of the rat.

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**IN MEMORIAM**



**JOHN HERR MUSSER, M. D.**  
**1883 - 1947**

JOHN HERR MUSSER, M. D.

1883-1947

WHEREAS, it pleased the Almighty God to remove from this earth Dr. John Musser, and

WHEREAS, Dr. Musser, a distinguished physician, scholar and educator, served the Louisiana State Medical Society faithfully and efficiently for many years as Editor of the New Orleans Medical and Surgical Journal, and

WHEREAS, as Editor of the Journal he contributed outstanding editorials, and numerous medical articles and papers which materially helped to maintain the high standard of the Journal, and

WHEREAS, he was taken from us to his Heavenly reward at a time when his advice and services were most beneficial to organized medicine,

BE IT RESOLVED that the Journal Committee feeling keenly the loss of a friend whose wise counsel, friendly attitude and scholarly attainments will be missed, expresses its deepest sympathy to the bereaved family in their great loss, and

BE IT FURTHER RESOLVED that these resolutions be spread in the minutes of this Committee and that a copy be sent to his family and published in the Journal.

THE COMMITTEE ON JOURNAL  
September 15, 1947.

In the death of Dr. John H. Musser we have lost another outstanding figure in our profession. The 64 year old Chairman of the Department of Medicine at Tulane University was a nationally known educator and a leading internist. He had been in failing health for the past two years; after a series of coronary occlusions he developed bloody pleural effusions requiring repeated thoracenteses. Despite this he continued to teach and was to have retired in June 1948 at the end of the forthcoming term. He was born in Philadelphia, in 1883, the son of Dr. John H. Musser, the fifty-sixth president of the American Medical Association. He came from a long line of doctors, his grandfather being Dr. Benjamin Musser, his great grandfather, Dr. Martin Musser, and his great great grandfather, Dr. Benjamin Musser. It was a great disappoint-

ment to him that his son who was tragically burned to death, did not follow the family medical tradition. He came to New Orleans in 1924 resigning the assistant professorship of medicine at the University of Pennsylvania to do so. It was from this university that he received his bachelor of arts degree in 1905 and his doctor of medicine degree in 1908. From 1911 to 1920 he was assistant editor of the American Journal of the Medical Sciences and editor from 1920 to 1924. He became editor of the New Orleans Medical and Surgical Journal in 1927, a position he retained until his death. He was very widely known as a writer, being the author of Musser's Internal Medicine, a text which went through four editions and was translated into several foreign languages. In addition he was the author of nearly 200 scientific papers. He had been a member and officer of most of the important medical associations in the United States, and a list of the organizations to which he belonged totaled 42. He was past vice president of the American Medical Association; he was a past president of the Louisiana Board of Health, the American College of Physicians and the New Orleans Graduate Medical Assembly. Locally also he was a member of the board of directors of the Child Guidance Center and president of the board of the New Orleans Institute for Mental Hygiene. During the first World War he served in France for one year with the rank of Major. He retained the rank of Colonel in the Medical Reserve Corps and during the second World War was a member of a committee appointed by the Secretary of War to study the reorganization of the Surgeon General's Office. He was an unfailingly courteous man who was entirely entitled to the affectionate title bestowed on him by his students: "Gentleman John." He had been visited by a series of cruel blows in his last days; these he met with an outward calm worthy of the classic Stoics. He is survived by his widow, the former Marguerite Hopkinson, a daughter, Mrs. Thomas L. Avegno, and four grandchildren. To these bereaved ones the Journal Committee extends its sincere condolences.



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## EQUINE ENCEPHALOMYELITIS IN LOUISIANA

The current epizootic of equine encephalomyelitis in the Lafayette area has resulted in the development of at least two human cases, one of which died and came to autopsy. Although final proof has not been established there is every clinical indication that the diagnosis is correct. For this reason recent laboratory investigation of the transmission of St. Louis encephalitis by a group of workers at Washington University becomes of immediate interest. Dr. Albert Miller of Tulane Medical School was one of this group. Present knowledge is to the effect that bird mites may maintain the virus in Nature and pass it on to their hosts. In birds the infection is symptomless. Mosquitoes feeding on such birds pass the virus in turn to man and other animals. Human and livestock epidemics apparently depend in part upon an abundance of mosquitoes in the area, along with the necessary virus in reservoir animals, which probably include chickens and other birds. The lack of specific therapy for human encephalitis makes imperative the acquisition of knowledge concerning its dissemination and prevention.

## ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

***An informed profession should be a wise one.***

## HEALTH WORKSHOPS

If possible every member of our State society, as well as the public, should read the recent House Report No. 786, 80th Congress, 1st Session, representing the Third Intermediate Report of the Committee on Expenditures in the Executive Depart-

ments. This is a summary of the Investigation of the Participation of Federal Officials in the Formation and Operation of "Health Workshops." These "Health Workshops" were special meetings held in various centers, called by Federal Agencies, for the purpose of planning propaganda, cre-

ating false issues and mapping a plan for support of the Murray, Wagner, Dingell measures for Federal insurance before Congress. These hearings were conducted by the above Committee during June and July 1947.

This factual report removes the lid of secrecy, and exposes by documental evidence the existence of one of the most powerful and astute propaganda groups to support President Truman's plan for Federalization of Medicine. It was not born overnight, but has developed in strength by continuous activity over many years. These active bureaus were found to be closely connected with foreign groups which were previously implicated in supporting governmental insurance in their respective countries. Especially aligned with this group was the International Labor Organization to whose efforts our administration in Washington has given its cooperation and tacit support.

Quoting from this report:—

The departments, bureaus, and agencies known to have participated in this campaign are:

1. The United States Public Health Service;
2. The Children's Bureau;
3. The Office of Education;
4. The United States Employment Service;
5. The Department of Agriculture; and
6. Bureau of Research and Statistics, Social Security Board.

Your committee finds that the use of Federal funds for the purpose of influencing legislation before Congress is unlawful under section 201, title 18, of the United States Code. We have, therefore, brought these matters to the attention of the Department of Justice, with a request that the Attorney General at once initiate proceedings to stop this unauthorized and illegal expenditure of public monies.

The spirit and purpose which dominates the officials of the United States Public Health Service in their campaign to high-pressure this legislation through Congress is reflected faithfully in the testimony of

Dr. Herman Hilleboe, Assistant Surgeon General, who appeared before the committee on May 28, 1947. He was asked by our committee chairman if the literature prepared by the Federal agencies offered all sides of the discussion or was limited merely to supporting material to carry out the President's order. To this question, Dr. Hilleboe answered:

"We would naturally give emphasis to that, because that is why we are in government. Otherwise, we should get out of government."

The same attitude of intolerance toward honest discussion or debate of the issue was indicated in the testimony of Mr. Harry J. Becker, health consultant in the United States Children's Bureau, Federal Security Agency.

Questioned as to the number of speeches he had made throughout the country in advocacy of the subject, the witness recalled several such appearances. Committee counsel, Frank T. Bow, pressed the inquiry (transcript of hearing, June 18, 1947, p. 228):

Mr. Bow: "Did you give both sides of the question of compulsory national health insurance when you gave your discussions?"

Mr. Becker: "I don't know what you mean by 'both sides'."

The Children's Bureau, Federal Security Agency, was represented in the health workshops movement by Mr. Harry J. Becker, a full-time employee of the Federal Security Agency, in the capacity of health consultant.

Here we have an exposé of the real agencies and bureaus which are leading an intrepid fight, through bureaucratic control, to thrust upon the American people compulsory insurance, contrary to the rights and privileges granted by our Constitution for free enterprise. Millions of dollars of your money and our money are being spent to carry on this lobby, with and by the support of agencies which should be above the level of practicing such politics, and which are merely presenting one side of a most controversial problem.

We all should hope that this report and



the Committee's findings, will not, like other Congressional investigations, die from ineptitude or political expedience, and that the recommendations of the Committee to the Attorney General, requesting action against those violating Section 201 of the U. S. Code for spending Federal funds illegally, will be prosecuted to the fullest extent, and that proper punishment will be meted out to those found guilty of such crimes.

Our executive officers and Congressional Committee have been cognizant of some of these group activities, while they pretended to be friends of American Medicine. Yet they are astounded at these revelations, thus demonstrating the formidable and subtle attack upon our medical profession and the unsuspecting public. It would not take a real honest interpreter or researcher in this field to evaluate and appraise the course for which our Government has set its sails.

What we can do about this exposure is the sixty-four dollar question. From an optimistic viewpoint, it is certainly an advantage finally to know your real enemies in this fight—there is now no room for conjecture, false rumors or doubts.

"The price of liberty is eternal vigilance". We should keep a scrutinizing eye on all the activities of these bureaus, lessen their infiltration into collaborating agencies of the state, and continue to fight for American Medicine in the true ethical manner so typical of our past. The public who, in the final analysis, will decide these matters, should be our ally. Our congressmen and senators should be made more aware of these forces and we should reaffirm to them our position. Their support and influence in Congress is imperative. Tell them what you think by personal contact or letter. It is not the time to be complacent.

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## ARE YOU WILLING TO HELP?

The members of the State Society will be interested to know that Louisiana Physicians Service, Inc., has attained a total en-

rollment during the past ten months of operation of approximately 20,000 persons, distributed over the entire state. It has, during the same period, paid to the physicians of Louisiana for the surgical and obstetrical care of these members approximately \$55,000.00.

It has gone through a very profitable but difficult period of acquiring definite information relative to the surgical and obstetrical needs of its members. This information is absolutely essential in order that the organization may eventually, on the basis of actual experience, be able to render the best service possible both to its subscribers and to the physicians of Louisiana.

The organization has proceeded on the principle that its function is to provide for all of its subscribers all of the services covered which they need and provide for the physicians rendering these services to receive adequate compensation for their services. It is equally true that for the people to have the services needed and the physicians to receive their compensation it is necessary that the premium payments shall be adequate to provide those services and maintain a reasonable cost-of-operation plus reserves for safeguarding the future of the company.

While the services rendered have far surpassed our expectations, we have been able to function in a fairly satisfactory degree through the cooperation and sponsorship of the State Society. It now becomes evident that to continue to render service on the scale as heretofore planned it will be necessary that there be an adjustment in our premium rates, for which some of the reasons, though obvious to anyone conversant with this problem, may be set forth in part as follows:

There is a general trend over the nation, apparent through exchange of ideas with representatives of other medical service plans, toward greatly increased utilization of both hospitalization and surgical care since January 1, 1947. The exact reason for this is not readily apparent but seems tied up with the changing times, the increased costs of living and a desire on the

part of the people to give more attention to their health care.

A second reason for the necessity of increasing our premium schedule arises from the greater liberality of our payments to physicians for services rendered . . . it having been the desire of our Board to approach as nearly as possible the prevailing minimum fees of the physicians of Louisiana for the care, particularly of the low-income group.

A third reason arises from the necessity of establishing branch offices in most of the principal cities of Louisiana and maintaining our own Home Office with complete records as required by our insurance department.

Because of these things, the Board now has under consideration and will shortly announce a change in rates to subscribers.

Besides the necessity of making this adjustment, which we consider a normal evolutionary process, our Board, in cooperation with the Council on Medical Service, is planning to launch a more intensive campaign to acquaint our doctors with the method of operation of the plan, including its limitations as well as its liberal features . . . and seeking to secure from the physicians a more active cooperation with the plan. It has become apparent through the servicing of the claims thus far that there are many reasons why physician cooperation is so essential and why there is need for so much more of it in reference to our plan.

A recent study by a committee on physician cooperation of the American Medical Care Plans brought to light several factors in securing such cooperation. While these are not listed in order of relative importance, some of the reasons for lack of cooperation are given as follows:

(1) The average physician does not understand how his own plan operates and does not regard the necessity for such understanding as important when compared with his own medical practice.

(2) Many physicians know little about how fee schedules are developed and may feel displeased unless the fee schedule fits

accurately his own conception of fees in his own practice.

(3) A third difficulty arises when the payments of claims to physicians are not carried out through medical personnel and at times resentment to inquiries for additional information left off the claim blanks has arisen.

(4) Some doctors apparently become irritated with the necessity of supplying factual information necessary to proper review of the claim preceding payment.

(5) It has been apparent in a few cases that physicians have rendered bills to patients for one amount and upon learning that they were covered by an insurance plan, have rendered our company bills in larger amounts. To be willing to do that in view of the fact that the physicians of Louisiana are operating the insurance company, raises the question of personal aggrandizement at the expense of other physicians. There must, therefore, be developed a strong spirit of cooperation and a highly disciplinary level within the ranks of the profession.

(6) The restrictions in our contract have invited some abuses and misunderstanding which stems again from a lack of realization of the necessity for such restrictions from an underwriting standpoint. This may create confusion, sometimes tempting doctors to falsify service reports to accommodate patients.

(7) Another need for increased cooperation arises from the physicians' secretaries needing to be taught the objectives and operating methods of the plan. Inasmuch as financial billing and other business arrangements are handled by such personnel, their relationship to the doctors and actual cooperation cannot be overlooked.

(8) It has been found that income limits for service benefits in some cases create confusion and an unwillingness on the part of the doctor to determine the patient's income is apparent from the large number of claim blanks being returned without this valuable information.

(9) One of our greatest difficulties



arises from the fact that doctors fail to read material directed to them through the mail because of the large amount of less important material which constantly clutters the physician's desk. Doctors can be taught to watch for mail from specified sources because it is related directly to his own practice of medicine—and it is hoped that any mail reaching a physician from our plan will have his immediate personal attention.

(10) It is axiomatic that doctors resist paper work and forms, but it is equally true that these have been reduced to the minimum essentials in handling our claims, and once the single-page claim blank is properly filled out there rarely would arise need for additional correspondence regarding the claim.

(11) Some physicians have shown a spirit of toleration of the plan as the lesser of two evils. If toleration could be changed to enthusiasm for it because of the service it is rendering the subscribers and the financial advantages accruing to the doctor through the proper use of the plan, we feel that real progress would be made. Doctors too often fail to appreciate the diverse and somewhat subtle processes through which public opinion is formed. It is therefore

highly important that the doctor's attitude display his firm support of the plan and present to the patient the conviction that his physician is supporting the plan for the good inherent in it rather than as the lesser of two evils.

These and many other factors in securing physician cooperation will be the subject of additional study by our own plan and those of every other medically-sponsored prepayment plan in the coming months.

At a recent meeting of the American Medical Care Plans held in St. Louis, these topics were considered of vital interest and definite planning is under way for the securing of better physician cooperation wherever such can be developed.

It is highly encouraging to know the rapid strides being made in the development of the physician-sponsored plans all over the nation, the enrollment now having gone well beyond six million—and the indications are that its increase will be much more rapid in the coming months.

When the physicians of Louisiana become committees of one to help solve some of the problems mentioned, our plan will be able to demonstrate progress comparable to that of the best and largest plans over the nation.

## TRANSACTIONS OF ORLEANS PARISH MEDICAL SOCIETY

- |          |   |          |   |
|----------|---|----------|---|
| Oct. 13. | Scientific Meeting, Orleans Parish Medical Society, 8 p. m. | Oct. 28. | Baptist Hospital Staff, 8 p. m.                                       |
| Oct. 14. | Orleans Parish Radiological Society, 8 p. m.                | Oct. 30. | Clinico-pathologic Conference, Touro Infirmary, 12 noon.              |
| Oct. 15. | Charity Hospital Surgical Staff, 8 p. m.                    | Oct. 31. | New Orleans Hospital Dispensary for Women and Children Staff, 8 p. m. |
| Oct. 16. | Clinico-pathologic Conference, Touro Infirmary, 12 noon.    | Nov. 3.  | Board of Directors, Orleans Parish Medical Society, 8 p. m.           |
|          | Veterans Administration Hospital Staff, 8 p. m.             | Nov. 4.  | Eye, Ear, Nose and Throat Staff, 8 p. m.                              |
| Oct. 17. | Executive Committee, Hotel Dieu, 8 p. m.                    | Nov. 5.  | Mercy Hospital Staff, 8 p. m.   |
|          | Lakeshore Hospital Staff, 8 p. m.                           | Nov. 7.  | Ochsner Clinic Staff, 8 p. m.   |
|          | The Orleans Society of X-ray Technicians, 7:30 p. m.        |          |   |
| Oct. 20. | Hotel Dieu Staff, 8 p. m.                                   |          |   |
| Oct. 21. | I. C. R. R. Hospital Staff, 12:30 p. m.                     |          |   |
|          | Charity Hospital Medical Staff, 8 p. m.                     |          |   |
| Oct. 22. | Catholic Physicians' Guild, 8 p. m.                         |          |   |
|          | French Hospital Staff, 8 p. m.                              |          |   |
| Oct. 24. | DePaul Sanitarium Staff, 8 p. m.                            |          |   |

### RADIO PROGRAMS

The Society, in cooperation with the Civic Affairs Committee of the New Orleans Association of Commerce, is planning to resume health talks over the radio in the very near future.

Those of you who are interested in appearing on these programs should submit your name and

the subject you would like to talk on to Dr. Val Fuchs, chairman of the Radio Committee. The Committee will assign you a date, and prior to your appearance you will be asked to prepare your talk in question and answer form and submit it to the Committee.

#### AMERICAN ACADEMY OF GENERAL PRACTICE

The general practitioners in the First District of Louisiana met August 20 and formed an Orleans Chapter of the American Academy of General Practice. It is the second Parish in Louisiana to organize.

The meeting was called to order by Dr. N. J. Chetta, councilor for the First District of Louisiana, who acted as temporary chairman until the election of officers.

Dr. J. P. Sanders of Shreveport, delegate from Louisiana to the national organization, was the principal speaker; he spoke on the aims and objectives of the AAGP.

Officers elected were: Dr. Joseph C. Menendez, president; Dr. E. A. Fatter, vice-president; Dr. R. E. Gillaspie, secretary-treasurer; Drs. E. L. Leckert, W. A. Gillaspie, Charles Moseley, Lucien C. Delery, Joseph J. Ciolino, Theo. F. Kirn, N. J. Chetta, George Barnes, and Frank Gallo, members of the board of directors.

Following the election of officers a committee was appointed to formulate a constitution and by-laws.

#### NEWS ITEMS

Drs. James E. Bailey, John Kometani, R. V. Platou, E. A. Socola and Alma Sullivan attended the recent meeting of the International Congress of Pediatrics in New York.

Dr. Platou presented a scientific exhibit on "Infantile Congenital Syphilis" at the meeting.

Dr. E. L. King attended the International Congress of Obstetricians and Gynecologists recently held in Dublin.

While abroad Dr. King visited various hospitals in London and Paris.

Dr. Roy H. Turner participated in a critique on the United States Army training course for regular army officers.

Dr. Turner was one of three who served as consultant on internal medicine at Brooks General hospital, San Antonio.

Dr. Ambrose H. Storck delivered two addresses at meetings of the Southern Pacific Railway Surgeons in Portland, August 29-30.

#### CHANGES OF ADDRESS

Dr. Branch J. Aymond, Jung Hotel.

Dr. A. F. Brock, 2008 Bodenger Blvd., Algiers.

Dr. Chester S. Fresh, 6237 So. Claiborne Avenue.

Dr. Thomas E. Furlow, 6210 Franklin Avenue.  
Dr. Joe Alfred Izen, 3606 Chestnut Street, Apt. C.

Dr. Edwin S. Kagy, 2618 Calhoun Street.

#### CHANGES IN MEMBERSHIP ROLLS

One member, Dr. Harry B. Caplan, was transferred from intern to active membership.

One active member, Dr. R. A. Oriol, was elected to inactive membership.

One active member, Dr. Thomas J. Walshe, passed away.

#### NEWS FROM NEW ORLEANS HOSPITALS

The resignation of Dr. Lewis E. Jarrett, director of Touro Infirmary, effective August 11, 1947, was announced earlier in the month by Mr. Eldon Lazarus, chairman of the board of the Hospital. Mr. Joseph M. Hinsley, Assistant Director and Controller of the Hospital, has been named acting director until a successor for Dr. Jarrett is appointed.

The construction of a new X-Ray Department at Touro Infirmary is near completion. The department which is located on the first floor of the Prytania Street wing of the Hospital should be one of the most up-to-date X-Ray establishments in the United States when it is completed. Work has also been started on construction of a Tumor Clinic at Touro. Announcement as to dates of the openings of these new facilities will be made sometime in September.

Sister Celestine, Administrator of Hotel Dieu, has announced the addition of a Personnel and Public Relations Department to the administrative staff of Hotel Dieu. This department began to function during July with John F. Screen as director of Personnel and Public Relations. The department will be responsible for recruitment and employment of workers, job analyses, salary and wage administration, maintenance of adequate personnel records, job evaluation studies and the development of a public relations program for the Hospital.

A new class of forty-four pre-clinical students was admitted to the Hotel Dieu School of Nursing on August 4th. This number just about reached the quota of 45 students which had been established for this class. Six states are represented in the class; 17 of the new students are from New Orleans and 17 from the State of Louisiana outside of the New Orleans area.

Appointment of J. V. Guillotte as Credit Manager of Hotel Dieu was also announced last week by Sister Celestine, Administrator of Hotel Dieu.



## LOUISIANA STATE MEDICAL SOCIETY NEWS

## C A L E N D A R

## PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

## SOUTHERN REGIONAL CONFERENCE

A number of national as well as regional individuals of prominence are scheduled to address the Southern Regional Conference to be held in New Orleans on Thursday, October 23, and Friday, October 24, at the Roosevelt Hotel, A. V. Friedrichs, M. D., Chairman of Arrangements, announced recently.

The conference is sponsored by the Council on Medical Service of the American Medical Association. Participating in the conference will be the Council on Industrial Health and the Committee on Rural Medical Service of the American Medical Association.

The States of Alabama, Arkansas, Louisiana, Mississippi, Oklahoma, Tennessee, and Texas are participating in the conference. Local arrangements for the conference are being handled by the Council on Medical Service and Public Relations of the Louisiana State Medical Society.

Appearing on the program will be Dr. George Lull, Secretary and General Manager of the American Medical Association, Dr. James R. McVay, Chairman of the Council on Medical Service of the AMA, Dr. Joseph F. Lawrence, Director of the Washington office of the Council on Medical Service of the AMA, Dr. Stanley J. Seeger, Chairman, Council on Industrial Health of AMA, and Dr. J. Paul Jones, Member of the Committee on Rural Medical Service of the AMA. Dr. G. C. Anderson, President of the Louisiana State Medical Society, and Dr. H. Ashton Thomas, President of the Orleans Parish Medical Society, will deliver the Addresses of Welcome. Many other prominent doctors and lay individuals of the South are also scheduled to actively participate in the Southern Regional Conference.

While the conference is primarily a meeting of the officers, directors, and committees of the various state and parish societies in the South, any doctor interested in the meeting is invited to attend.

## THE FOUNDATION HOSPITAL

A meeting of the Staff of the Foundation Hospital was held on Friday, September 5, 1947 at

8 p. m. at the hospital. A symposium was held on Lumbosacral Anomalies in Relation to Low Back Pain with the following doctors presenting various subjects: Embryology and Evolution, Dr. Joe W. King; Mechanical Effects, Dr. Richard Shorkey; X-ray Definition, Dr. Richard Boyer; Symptoms and Signs, Dr. W. Bostwick Sheppard; Relation to Disc Problem, Dr. Alfons R. Altenberg; Treatment, Dr. George G. Gill.

## ADDITIONAL FUNDS FOR CORONER'S OFFICE

Mayor Morrison announces that an additional appropriation of \$1500 will be made in the budget of the Coroner's Office to purchase needed equipment. The Mayor, in discussing this recommendation, states that "serious errors in autopsies have been made in the last few months, and I am informed that these errors are the results of improper and inadequate equipment."

## TULANE MEDICAL REGISTRATION

There are 476 students registered in the Tulane University School of Medicine for the coming year. In addition to the regular courses there will be ten full time and two part time students in the nine month public health (tropical medicine) course which will be given in the Division of Graduate Medical Studies.

## MAGRUDER HONORED

Dr. Marcus J. Magruder, who has been a member of the staff of Touro Infirmary for more than sixty years, on Wednesday, September 3 was made a life member of the medical staff at exercises held at his bedside. Dr. Magruder is recuperating from an eye operation.

Mr. E. S. Lazarus, president of the Hospital Board of Supervisors, described Dr. Magruder when he handed him the plaque, saying he had been given a lifetime appointment at the hospital as one of the few old time family doctors.

This plaque has been given to only two members of the Touro staff, Dr. Rudolph Matas and Dr. Magruder. Dr. Magruder gave a short talk in

which he said that when he came on as an intern at Touro there were only two in the group, there were no graduate nurses not only at Touro but in any hospital in the city.

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#### DR. DUPUY HONORED

Received as a member of the French Legion of Honor, Dr. Homer J. Dupuy was decorated September 10 with the medal of the order "for extraordinary service" rendered in directing medical facilities for 40,000 French troops at Taranto, Italy prior to their invasion of Southern France in 1944. The medal was presented by Consul General Jean Lapierre of France in ceremonies at the French Consulate in New Orleans.

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#### LOUISIANA STATE UNIVERSITY SCHOOL OF MEDICINE

The School of Medicine, Louisiana State University, has expanded its school year from 32 to 36 weeks and the following new appointments have been announced: Dr. Harry E. Dascomb, Instructor in Medicine (assigned to Microbiology); Dr. Robert M. Waters, Instructor in Surgery; Dr. John J. Blasko, Clinical Instructor in Neuropsychiatry; Dr. Louis Raider, Clinical Instructor in Radiology; Dr. Simon V. Ward, Jr., Clinical Instructor in Obstetrics and Gynecology; Dr. Harold S. Gamble, Assistant in Anatomy; Dr. John D. Krafchuk, Assistant in Microbiology; Dr. James T. McQuitty, Clinical Assistant in Surgery; Dr. Robert D. Bone, Clinical Assistant in Medicine.

Registration of 310 students in the medical school has taken place. These include 98 new students; 91 men and seven women. Fifty-four are veterans. Three are from Latin America.

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#### NEWS ITEMS

Dr. Rudolph Matas and Dr. Isidore Cohn attended the 12th International Surgical Congress September 14-20 in London. Dr. Matas served as president of the last congress, held in 1938 in Brussels, Belgium, after having been elected in absentia at the 1936 congress in Cairo, Egypt.

Dr. William H. Block has been awarded life membership in the Medical Alumni Association of the University of Maryland. Dr. Block graduated from the University of Maryland in 1895 and is entitled to life membership since the Alumni Association recently passed a resolution that all members would be granted this honor after having reached the fiftieth anniversary of their graduation.

Dr. Manuel Garcia was re-elected president of the Orleans Parish Unit, American Cancer Society, at the meeting held Wednesday, September 3. Dr. Walter Levy was re-elected secretary and Dr. M.

S. Steege, Jr., treasurer. Mrs. C. C. Walther was selected as vice-president.

The report of the Hutchinson and Louisiana State University Cancer Detection Clinics were presented at the meeting. In the Hutchinson Clinic of 323 people examined, 12 cases of cancer were discovered; at the L. S. U. Clinic of 299 racially mixed patients there were seven cases of this disease detected.

The results of these two clinics will exemplify what can be done in cancer prevention, as undoubtedly the cases that were diagnosed may be treated and helped.

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#### AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY

The sixth annual meeting of the American Academy of Dermatology and Syphilology will be held in Chicago December 6-11. Principal sessions will be held at the Palmer House with special courses in histopathology and mycology scheduled at the medical schools of the University of Illinois and Northwestern University and teaching clinics at the University of Illinois College of Medicine.

Extensive scientific and technical exhibits will be set up in connection with the meeting. Dr. Marcus R. Caro, of Chicago, heads the committee on scientific exhibits and Dr. Clyde L. Cummer, of Cleveland is in charge of the technical exhibits.

Special courses in histopathology, mycology, x-ray and radium therapy, bacteriology of the skin, mucous membrane lesions, industrial dermatoses, specific granulomata, and dermatoscleroses will be held under leaders in these various fields. Subjects to be discussed in symposia will include: physiology and chemistry of the skin; physical and radiation therapy; cutaneous allergy; syphilis; pharmaceutical therapeutics; and diagnostic methods in dermatology. Other features will be a round table discussion on dermatopathology and a panel on management of skin diseases.

Lectures will be given by Dr. G. H. Bishop, professor of neurophysiology, Washington University, Dr. Harvey Blank, University of Pennsylvania and Dr. A. C. Ivy, Vice-President of the University of Illinois.

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#### THE AMBULATORY FRACTURE ASSOCIATION

Announcement has been made that the Eighth Annual Meeting of the Ambulatory Fracture Association will be held in Aurora, Illinois, October 9-11, 1947, with convention headquarters at the Leland Hotel. The program will follow the usual pattern with the presentation of papers, case reviews, operative and dry clinics, dealing chiefly with fractures and traumatic injuries.

From October 13 through 17 there will be study classes on skeletal fixation technics, sponsored by the Association. These classes will be limited to



50 persons. For detailed information communicate with the office of the Association, 120 South La Salle Street, Chicago 3.

#### THE NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

A three-day conference will be held April 5-7, 1948 by the National Society for the Prevention of Blindness at the Hotel Radisson, Minneapolis. Persons who are directly or indirectly concerned with eye health and safety are invited to attend this conference, detailed program of which will be available at a future date.

#### OFFICE SPACE FOR DOCTOR

Information has been received by the office of the Journal that there is available office space for a doctor at 4402 Jefferson Highway, New Orleans.

#### HEALTH OF NEW ORLEANS

The Bureau of the Census, Department of Commerce, from the figures reported by the New Orleans Health Department, announces that there were 173 deaths occurring in the City of New Orleans during the week which ended August 9. These deaths were divided 115 white, 58 nonwhite and included 27 children under one year of age. There was a slight decrease in number of deaths reported for the week ending August 16, the total number being 149 with only 12 infant deaths. One hundred and three white persons and 46 colored persons expired this week. The next week, which closed on August 23 showed a further decrease in number of deaths in the City of New Orleans. The same number of colored persons died, however there were only 81 deaths in the white population reported, which was a decrease of 22 in the figure recorded for the previous week. The total number of deaths reported for the week which ended August 30 was 137; an increase of ten over the week of August 23. Ninety-five of these occurred in the white race and 42 in the nonwhite, with ten infant deaths reported.

#### INFECTIOUS DISEASES IN LOUISIANA

The weekly morbidity report for the State of Louisiana for the week ending August 2 included 103 cases of cancer, 49 of unclassified pneumonia, 23 of pulmonary tuberculosis, 20 each of pneumococcal pneumonia and septic sore throat and 15 of measles. There were two cases of malaria reported this week; one contracted within the Continental United States and one outside of Continental United States. No cases of poliomyelitis were reported this week. The number of cancer cases dropped to 71 the week ending August 9, however there was an increase in the number of cases of pulmonary tuberculosis, there being 80 instances of this disease recorded in the state this particular

week. The only other disease reported in number greater than ten was unclassified pneumonia with 25 cases. Three cases of poliomyelitis were reported, one each from Caddo, Orleans and Rapides Parishes and a total of six cases of malaria; five of which were contracted within the Continental United States. One case of meningococcus meningitis was also reported from Orleans Parish. Amebiasis led all reportable diseases in the state for the week ending August 16, with 65 cases reported. This disease was followed by 53 cases of cancer, 42 of pulmonary tuberculosis and 20 of unclassified pneumonia. The number of malaria cases was decreased to two; place of contraction not stated for one and the other contracted within Continental United States. Again, one case of meningococcus meningitis was reported from Orleans Parish. There were only two diseases reported in numbers greater than ten for the week ending August 23; 43 of cancer and 30 of unclassified pneumonia. Two cases of malaria, contracted outside of the Continental United States were reported and one case of meningococcus meningitis occurred in Acadia Parish.

#### MONTHLY MORBIDITY FOR VENEREAL DISEASES, STATE OF LOUISIANA

Month Ending July 31, 1947

	Total This Month	Total Previous Months	Total To Date 1947
Lymphopathia Venereum	13	41	54
Chancroid	43	329	372
Gonorrhea	1367	7397	8764
Granuloma Inguinale	18	105	123
Syphilis	989	5768	6757

#### CHARLES J. BLOOM

1886-1947

Dr. Charles James Bloom, nationally known New Orleans pediatrician died at Touro Infirmary on August 28. Dr. Bloom received his doctor of medicine degree from Tulane University in 1912 and was honor man in the class taking examinations for medical licenses. He continued his medical studies at Harvard where he did graduate work from 1914 through 1916. Following completion of his university work, Dr. Bloom devoted the rest of his life to child welfare, as a working pediatrician as well as a teacher and writer on topics related to infant care. He was the author of "The Care and Feeding of Babies in Warm Climates" and of numerous articles for medical journals. Many staff appointments were held at various New Orleans hospitals by Dr. Bloom, including co-chief of the Department of Pediatrics at Mercy Hospital; senior staff member at Touro Infirmary; pediatrician

in charge of the the Lying-In Hospital; staff member at Southern Baptist Hospital; senior visiting pediatrician at Charity Hospital, Hotel Dieu, Presbyterian Hospital and the New Orleans Dispensary for Women and Children; consulting pediatrician at the French Hospital; and chief of pediatrics at Flint Goodridge Hospital.

During World War I he was a consultant in pediatrics for the American Red Cross and also served as a First Lieutenant in the Medical Reserve Corps.

His teaching work consisted of instruction at Tulane University, where he was professor of pedi-

atrics and head of the postgraduate medical department from 1916 to 1937; Louisiana State University where he was department head and professor of pediatrics from 1937 to 1940; and the Southern Pediatric Seminar, Saluda, North Carolina, where he was a faculty member from 1924 to 1942.

In 1935 Dr. Bloom served as president of the Louisiana Pediatric Society. In addition to that organization he was a member of the Orleans Parish Medical Society, Louisiana State Medical Society, Southern Medical Association and American Medical Association.

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## BOOK REVIEWS

*The Treatment of Diabetes Mellitus:* By Elliott P. Joslin, A. M., M. D. Sc. D., Howard F. Root, M. D., Priscilla White, M. D., Alexander Marble, A. M., M. D., and C. Cabell Bailey, M. D., 8th ed., Philadelphia, Lea and Febiger, 1946. Pp. 861. Illus. Price, \$10.00.

The eighth edition of this comprehensive work maintains the preeminence established by earlier editions as a standard for all phases of consideration of the clinical features of diabetes mellitus. As the author states in his preface "It is easily seen that this expansion (of the field of diabetes) has necessitated too much detailed knowledge for one doctor." He could hardly have chosen better than to include as co-authors who worked with him in developing the program of the George F. Baker Clinic.

In general, the book follows the pattern set by its predecessors. The growing number of diabetics is stressed; that they mature and incur the same illnesses as do nondiabetics of their respective age groups has led to the inclusion of much new material, a considerable portion of it devoted to the problems of obstetrics and geriatrics. A new chapter on "Alloxan Diabetes" describes some of the experiments by which animals can be rendered diabetic within a few minutes after a single injection of this chemical and implies that clinical application may soon be realized. Inasmuch as life insurance companies are now considering the practicability of issuing life insurance to diabetics, the

sections on statistics becomes even more important than formerly.

Those who have come to rely on Joslin's text for guidance in the management of the diabetic patient will find this edition as helpful as those which preceded it. Some may take issue with a few of Joslin's dogmatisms; e. g., his insistence that the intravenous administration of glucose is harmful and that alkalies are useless in diabetic acidosis. Despite this the general practitioner, for whom the book is primarily intended, will find that the methods detailed are sound, practicable and applicable to by far the majority of incidents apt to be noted in the "careers" of diabetics.

SYDNEY JACOBS, M. D.

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*Penicillin in Syphilis:* By Joseph Earle Moore, M. D. Springfield, Ill. Chas. C. Thomas Co. 1946. Pp. 319. Charts. Price \$5.00.

"Penicillin in Syphilis" is a volume comprising a condensation of voluminous literature on penicillin and its effect on syphilis. The author, in his typically clear and orderly manner, reviews the chemistry, pharmacology, therapeutic activity and the mechanism of action of penicillin. He then discusses the action of penicillin and its results, as far as is presently known, on syphilis of the various systems of the body.

The authoritative crystallization of the latest thoughts and experiences on this important subject



makes the book invaluable to all interested in the treatment of syphilis. The excellent review of the fundamentals of penicillin and its actions will make this edition popular with all physicians. The book is recommended to all physicians and medical students.

JOHN G. MENVILLE, M. D.

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*Principles and Practice of Obstetrics:* By J. B. DeLee, M. D., and J. P. Greenhill, M. D. 9th ed. Philadelphia, W. B. Saunders Co., 1947. Illus. figures, pl. pp. 1011. Price, \$10.00.

In revising DeLee's *Principles and Practice of Obstetrics*, Dr. J. P. Greenhill has added much new material in the ninth edition of this well-known textbook. This has been accomplished by adding new chapters on "Minor Disturbances of Pregnancy," "Diagnosis of Post-Maturity and Missed Labor," "Erythroblastosis" and "Prematurity," although this book is 100 pages shorter than the eighth edition.

There are a total of 1,108 illustrations, 211 being in color, representing an increase over the previous edition. Many of our newer ones are excellent reproductions showing anatomy and pathology relative to obstetrics. As would be expected, local analgesia is stressed over general and spinal, as the method of choice for both normal and operative delivery. Many additions have also been made to the sections dealing with diseases of the blood and surgical procedures, hyperemesis gravidarum, toxemias of pregnancy, postpartum hemorrhage, placenta previa, abruptio placenta, and chronic infectious diseases complicating pregnancy.

The high position of this book as a modern and complete exposition of obstetrics is fully maintained, as evidenced by the fact that it is the choice of the Obstetric Department at Tulane for undergraduates in the School of Medicine.

C. M. JOHNSON, M. D.

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*Paravertebral Block, Its Diagnosis, Prognosis and Therapy; Minor Sympathetic Surgery:* By Felix Mandl, M. D., F. I. C. S. New York, Grune & Stratton, 1947. Illus. Pp. 330. Price, \$6.50.

This book of 330 pages including the index covers the field of paravertebral block, the discussion including the indications for this form of therapy, the technique of the method, and the end results.

It summarizes, in fact, the author's personal experience and the experience of other observers with this method over the past quarter of a century. The possibilities of paravertebral block are clearly presented, though more emphasis might have been put on its relative as well as its absolute advantage.

The book would have been improved by judicious condensation. It is almost too voluminous for the factual matter presented. The illustrations are not original and are not particularly well reproduced. The translation, from the standpoint of readability, is excellent. The most valuable feature of the book is perhaps the complete bibliography.

ERNEST G. DEBAKEY, M. D.

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*Effect of Smallpox on the Destiny of the American Indian:* By E. Wagner Stearn, Ph. D., and Allen E. Stearn, Ph. D., Boston, Bruce Humphries, Inc., 1945. Pp. 153. Price, \$2.50.

Presenting an epidemiological study of smallpox in the American Indian, this volume is also a contribution to our national history. It shows the undoubted advantage which the ravages of smallpox on a non-immune native people, gave to our early settlers, and the great influence which this balance of power had on the development of this country. The study is well documented throughout by citation of source reference. It may well serve as an authentic reference work on the history of smallpox, that dread scourge which decimated our population prior to the discovery and obligatory practice of vaccination.

MARY LOUISE MARSHALL.

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*Diseases of the Chest: Emphasis on X-ray Diagnosis:* Eli H. Rubin, M. D., F. A. C. P., F. C. C. P., Philadelphia, W. B. Saunders Co., 1947. Pp. 685. Price, \$12.00.

There has long been a need for a book on diseases of the lungs which can be recommended to senior medical students, postgraduate students and general practitioners, as a thorough and modern presentation of this special field in one volume. This book answers that purpose admirably. Beginning with a section on basic anatomy, roentgenology, pulmonary tuberculosis, other chronic pulmonary diseases and conditions of the pleura, mediastinum and diaphragm. An excellent section summarizing the present status of surgical treatment is contributed by the principal author's brother, Morris

Rubin. The book's strength as well as its one possible defect is indicated by the subtitle. The emphasis on roentgenologic diagnosis is in accord with modern practice and the illustrations from hundreds of roentgenograms make this volume an unsurpassed x-ray atlas of the thorax. Incidentally, the reproduction of these completely excellent roentgenograms is of superior quality as is the format of the book. If any criticism can be made of the text, it is that examination of the patient and certain physical signs are rather slighted. The explanations offered for some of the signs mentioned are not generally accepted. There are excellent bibliographies at the end of each chapter. As suggested in the preface, radiologists will find this book valuable to furnish background for their interpretation of chest roentgenograms. General practitioners and students can now obtain an up-to-date and authoritative work on diseases of the chest which will be a most useful addition to their library for daily use. To all such this book is recommended highly.

JULIUS LANE WILSON, M. D.

*History of the American Medical Association, 1847 to 1947:* By Morris Fishbein, M. D. and others. Philadelphia, W. B. Saunders Co. 1947. Pp. 1226. Illus. Por. Price, \$10.00

Published in recognition of the 100th anniversary of the American Medical Association, this exhaustive compilation will furnish for physicians, for libraries and for the public an authoritative reference source on the development of American medicine for the past century, as it has been lead and influenced by this great medical organization. Particular attention is given to the contribution of the Association in raising standards of medical education, in eliminating quackery, in improving industrial health and in promoting a wide distribution and high quality of medical care.

In addition to a chronologic account of the general activities of the Association, from its organization in 1847 to the present time, there will be found biographic sketches and portraits of its founder, Dr. Nathan Smith Davis, of its 101 Presidents and of the nine recipients of its Distinguished Service Medal, first of whom was our own Dr. Rudolph Matas.

Included also are historical accounts of the special individual activities of the American Medi-

cal Association, its Councils and Bureaus, its Library, the Committee on Scientific Research, the Woman's Auxiliary, the Association's scientific sections and its publications. Full indices of persons and of subjects add greatly to the book's future usefulness.

MARY LOUISE MARSHALL

*Tuberculosis As It Comes and Goes:* By Edward W. Hayew. Privately published by the author. Monrovia, California, 1943. Pp. 187. Illus. Price, \$2.00.

This small book contains a wealth of information about tuberculosis for the average patient who must combat this illness. Organized into a number of short chapters, each with a brief title and aptly-chosen subtitle (Chapter V., for example is headed "Infection versus Disease" and sub-headed "many are called but few are chosen") a graphic portrayal of the clinical features of tuberculosis and its forms of therapy is presented. The inclusion of a large number of diagrams makes it easy for the inquiring patient to learn what is scheduled for him and how it is to be accomplished.

Using a minimum of technical language to convey a maximum of information, Dr. Hayes has provided a little book which would well repay the general physician or surgeon for the reading. Like so many other "manulas" presented to the non-professional reader, it deserves a prominent place on the book shelf of the busy doctor.

SYDNEY JACOBS, M. D.

#### PUBLICATIONS RECEIVED

Chemical Publishing Co., Inc., Brooklyn: Colloid Science, A Symposium by E. K. Rideal, A. E. Alexander, D. D. Eley, P. Johnson, F. Eirich, R. F. Tuckett, J. H. Schulman, M. P. Perutz, G. S. Adair, G. B. B. M. Sutherland, and R. R. Smith.

The Commonwealth Fund, New York: Hospital Care in the United States, report of the Commission on Hospital Care.

Grune & Stratton, New York: Introduction to Medical Psychology, by L. Erwin Wexberg, M. D.

Lea & Febiger, Philadelphia: A Hand-Book of Ocular Therapeutics, by the late Sanford R. Gifford, M. D., F. A. C. S. and revised by Derrick Vail, M. D., D. O. (Oxon), F. A. C. S.

J. B. Lippincott Company, Philadelphia: New



and Nonofficial Remedies, 1947, Issued Under the Direction and Supervision of the Council on Pharmacy and Chemistry of the American Medical Association.

The C. V. Mosby Company, St. Louis: Infant Nutrition (4th ed.), by P. C. Jeans, A. B., M. D. and Williams McKim Marriott, B. S., M. D.; Synopsis of Allergy (2nd ed.), by Harry L. Alexander, A. B., M. D.

W. B. Saunders Company, Philadelphia: Internal Medicine in General Practice (2nd ed.), by Robert Pratt McCombs, B. S., M. D., F. A. C. P.; The American Illustrated Medical Dictionary (21st ed.), by W. A. Newman Dorland, A. M., M. D., F. A. C. S.

Charles C. Thomas, Springfield, Illinois: Ocular Therapeutics, by William J. Harrison, Phar. D., M. D., F. A. C. S.

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1947-1948

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 Revision of By-Laws: Mrs. L. H. Pirkle, 865 Margaret Place, Shreveport.  
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# A MESSAGE TO THE WOMAN'S AUXILIARY

My greatest regret in life is that I am not able to claim credit for establishing the Woman's Auxiliary to the Louisiana State Medical Society. The records, however, will show that in 1923, while President of the Louisiana State Medical Society, I asked that the Society sponsor such an organization, and appointed a committee to establish an Auxiliary. The committee reported on the last day of the convention, that it was not advisable at that particular time to sponsor an organization of this type. And it remained for some other president to be the means of forming an organization, that has been of so much value to "organized medicine." The work that these loyal and energetic women have accomplished has meant much to the physicians of Louisiana individually and to the Society collectively.

To Mrs. Arthur D. Long, who served as President during the past year, go my thanks for her splendid co-operation and my congratulations for her accomplishments. It was a privilege to be associated with one who entered into the work with so much enthusiasm, energy and real executive ability.

May I thank the Woman's Auxiliary for allowing me the privilege of serving as Chairman of the Advisory Board, a position that has meant much to me, particularly as it enabled me to see the valuable aid that this group of wonderful women gave to the Disciples of Aesculapius.

LESTER J. WILLIAMS, M.D.,  
 Chairman, Advisory Council,  
 1946-1947.

## MESSAGE OF PAST PRESIDENT OF WOMAN'S AUXILIARY

Dear Auxiliary Members:

As doctors' wives and Auxiliary members, we face an ever expanding program if we are to keep pace with the changing times and be of any real service to our doctor husbands. In spite of tremendous strides in medical science, the profession faces charges that it has neglected or ignored the social and economic aspects of medicine, and that, though an idealistic profession, it has been apathetic or has refused to take realistic action in providing for more adequate distribution of medical services.

It makes no difference that these charges are untrue!

It remains that the people have come to believe that the health of the individual is a public responsibility, that the individual's ability to pay should have no bearing on the quantity or quality of medi-

cal care he receives, and moreover,—through propaganda, aided by the constantly growing trend toward a paternalistic and bureaucratic system,—many think that this care should be provided at public expense.

The principles of this philosophy are reflected in the multitude of proposed health bills, such as the WMD bill, whose passage would bring about the regimentation of medicine under governmental control.

Aroused public opinion eventually will demand the passage of such legislation unless we can expose this Utopian dream for the tragic fraud it is. The people have been the dupes of great masses of misinformation concerning the benefits of State Medicine. But to mould public opinion one must be convincing, and to be convincing one must have convictions! It is necessary to know the history and background of this movement, to be apprized of its faults and fallacies, and to acquire the ability to present the merits of our alternative. Vague theorizing and mere prejudice will not suffice. We must know the arguments of both sides to be able to refute the proponents of political medicine, and we must offer the public a better solution to their medical needs. We have this solution in the Louisiana Physicians' Service plan.

When we comprehend fully the insidious aspects of the crises threatening the medical profession, I think every Auxiliary member will feel it her duty in her daily contacts to use her knowledge to promote the widest acceptance of the Physicians' Service plan. As the public learns that the medical profession is neither indifferent to the patient's economic needs nor primarily concerned with its own financial gain, much confidence and goodwill will be restored.

The following books, which are only a few of the many you will find on the subject on the shelves of the public libraries, will give an insight into the problems facing us:

FREE MEDICAL CARE—E. C. Buehler (text for debaters).

HEALTH IN HANDCUFFS—John A. Kingsbury.

MEDICINE AT THE CROSSROADS—Franz Goldman, M.D.

THE DOCTOR AND THE PUBLIC—James P. Warbasse, M.D.

Only as we are informed can we fulfill our responsibilities as doctors' wives.

With complete confidence that you will continue to give your enthusiastic cooperation to the incoming officers that you so graciously gave to me, I wish to express again my gratitude for the privilege of having served as your president.

Most sincerely,

MARGARET STEWART LONG.  
 (MRS. ARTHUR D. LONG).

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1947-1948

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1947-1948

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Preservation of Medical Cultural Items

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### CIRCUMVALLATE PLACENTA\*

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The subject of circumvallate placenta does not appear frequently in the obstetric literature. One of us (A.B.H.), who previously had become interested in this subject through the suggestion of W. J. Dieckmann, discussed it in 1935 and reported two cases.<sup>1</sup> Since then, our interest in this subject has prompted closer inspection of placentas and has led to the collection of additional data, particularly of data relating to clinical symptoms and fetal mortality.

In approximately half of the instances of circumvallate placenta that we have observed, the symptoms somewhat resembled those of placenta previa or of premature separation of the placenta. We, therefore, feel that it is worthwhile at this time to compare the symptoms of these three conditions. In several instances, circumvallate placenta occurred in more than one pregnancy in the same case. Its co-occurrence with placenta previa also has been noted.

Circumvallate placenta is an anomaly which has been of interest to obstetricians chiefly from anatomic and pathologic viewpoints. Williams,<sup>2</sup> Goodall<sup>3</sup> and others have written complete descriptions of this anom-

aly, have cited the theories of other authors as to its formation and have advanced their own plausible theories for its pathogenesis. Williams<sup>2</sup> quoted various German writers, notably Herff, Bayer, Seitz and others, who said that obstetric complications, such as abortion, unexplained bleeding, premature labor and anomalies of the third stage of labor, may result from circumvallate placenta. However, both Williams and Schumann stated that in their experience the anomaly had no clinical significance. On the contrary, Hobbs and Rollins<sup>4</sup> who, in 1934, reviewed their observations in 79 cases of this condition in a period of 13 years found that obstetric complications were present in 39 of the cases. The fetal mortality rate in their series was 43 per cent, which is higher than that for most obstetric conditions except perhaps for abruptio placentae, severe toxemia and rare instances of rupture of the uterus.

We shall review briefly the derivation of the term "circumvallate placenta," the probable pathogenesis of the condition and the anomalous structure to which its symptoms appear to be related. It will be recalled that the entire surface of the embedded amniotic sac is covered with villi which exhibit a profuse growth usually in the area most closely approximated to the uterine wall. As the placenta develops, that portion of the chorion which overlies this profuse growth is called the "chorion frondosum" while the part of the chorion from which the villi have atrophied and disappeared is called the "chorion laeve." The chorion frondosum has a smooth glistening fetal surface which is called the "placental plate."

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The placental plate has definite limits, the extent of which is determined by several factors which will not be considered here. The normal growth of the chorionic placental plate is determined usually by the size of the placental site, which in turn is related to the growth of the uterus and its contents.

The life cycle of the placenta covers a scant nine months. In the course of this time, as Goodall has aptly stated, the placental growth encompasses a life time—childhood, adolescence, maturity and senility. In some placentas, as in tissues of the body, degenerative changes may occur relatively early. In fact, infarction and sclerotic changes, which may appear early in gestation along the border of the placental plate, tend to interfere with the blood supply so that growth of the placental plate cannot keep pace with the increase in size of the growing placental site. In such cases, an outgrowth of villi may extend beneath and beyond the border of the chorion frondosum as an expression or attempt on the part of the placenta to maintain its function of nourishing the fetus. This outgrowth of villi causes them to pile up beyond the limits of the chorion frondosum and here they are covered by the chorion laeve, which is thus raised up from the wall of the uterus and put under tension by the vigorously growing villi. As this piling up of villi occurs outside the more or less fibrous limit of the chorion frondosum or placental plate, it may partially or completely surround the circumference of the placental plate with a mass of villi which is elevated above the level of the plate and gives rise to the term "circumvallate." It is along this circumference that the increasing tension may cause a tear in the tissue and produce bleeding and sometimes seepage of amniotic fluid.

#### INCIDENCE

Forty-seven instances of circumvallate placenta were observed among 8,861 consecutive deliveries on the service of the Section on Obstetrics and Gynecology of the Mayo Clinic from January 1, 1934 to December 31, 1946, inclusive. Prior to Jan-

uary 1, 1934, we had not always been alert to observe and record cases in which this anomaly was present and it is quite probable that some instances may have been overlooked since that date and that many more than 47 instances actually occurred. However, it is probable that the condition of the placenta was noted in all cases in which symptoms were produced. This supposition is strengthened by Hobbs and Rollins<sup>4</sup> who reported finding this anomaly in 79 cases. In only 45 of these cases was the pregnancy at or near term. Hobbs and Rollins also noted a ratio of one instance of circumvallate placenta in 50 pregnancies while we recorded one in 188 pregnancies.

In 23 of the 47 instances, the anomaly did not produce any clinical symptoms. These 23 instances of the anomaly occurred in 22 cases. The 24 instances of the anomaly which produced symptoms occurred in 19 cases; two instances of the anomaly occurred in each of three cases and three instances occurred in one case.

In standard textbooks on obstetrics, scant mention, if any, is made of the clinical importance of circumvallate placenta. This may be due to the fact that the anomaly frequently does not produce any symptoms that are of clinical importance. As we have just stated, there were no important symptoms in 23 of the 47 instances of this anomaly observed at the clinic. In these 23 instances, the duration of gestation averaged 39 weeks and a fetal death occurred in only one instance. In this instance, the fetus died three weeks before delivery. A history of bleeding was obtained in only two of the 23 instances. In each of these two instances, the bleeding occurred prior to the fourth month of gestation. On the other hand, in 15 of the 25 instances in which the anomaly produced symptoms that were considered important clinically, bleeding or spotting with blood or drainage of fluid occurred before the fourth month of gestation.

In nine instances, including some of those in which early bleeding persisted or recurred, uterine bleeding occurred in the last half of pregnancy. In seven instances the bleeding was due to circumvallate placenta,



while in two instances placenta previa also was present. In these two instances, the placenta previa was undoubtedly of greater importance clinically. Placenta previa is encountered in approximately one of every 200 pregnancies. Since it occurred in two of the 47 instances of circumvallate placenta, one may question whether some factor affecting nidation may not be an etiologic factor in both conditions.

In five of the seven instances just mentioned, the bleeding was of such severity, grade 2 to grade 3 (on the basis of 1 to 4) that it was thought, in the prepartum period, to be caused by premature separation of the placenta.

In 15 instances, the amniotic sac ruptured spontaneously preceding the onset of labor. In the majority of these instances, it ruptured before the thirty-fourth week of gestation; in seven instances, fluid (hydorrhea gravidarum) drained for from one to ten weeks prior to the onset of labor, which in each instance was premature. Examination of the placenta indicated that, in all probability, tearing occurred at the fibrous ring which marks the border of the chorion frondosum or placental plate and that this was caused by the continuing growth of placenta while the insertion of the membranes remained stationary.

Rupture of the membranes preceding the onset of labor, which occurred in 15 or a third of the 47 instances, or in three-fifths of the instances in which symptoms were present, is of distinct clinical importance because it usually is followed by premature labor and commonly by death of the prematurely born infant.

In the 24 instances in which the circumvallate placenta produced symptoms, the fetal mortality was 50 per cent. The mortality was chiefly attributable to prematurity although some extremely premature babies survived as indicated in table 1. The fetal mortality rate in the 47 instances was 24 per cent. There were no maternal deaths although one patient (who did not have placenta previa) required a transfusion of blood.

TABLE 1

ONSET OF LABOR AND FETAL SURVIVAL IN  
TWENTY-TWO INSTANCES OF CIRCUMVALLATE  
PLACENTA WITH CLINICAL SYMPTOMS\*

Onset of labor, weeks	Instances	Fetal survival
20 to 24	3	0
25 to 29	5	0
30 to 34	5	2
35 to 38	5	5
39 to 40	4	4
Total	22*	11 (50 per cent)†

\*Two instances in which placenta previa was associated with circumvallate placenta have been excluded from this table.

†The fetal survival rate in the entire 47 instances of circumvallate placenta was 74 per cent.

When uterine bleeding occurs during pregnancy, it is necessary to determine, if possible, the cause of the bleeding, and it is especially important to rule out the more serious causes of maternal hemorrhage, that is, placenta previa and abruptio placentae. This usually can be done readily by the history and by careful physical and roentgenologic examination. Roentgenologic examination has not proved to be of accurate value before the eighth month of gestation. Table 2 shows the distinguishing features of cir-

Table 2

DIAGNOSTIC FEATURES OF CIRCUMVALLATE  
PLACENTA AND PLACENTA PREVIA

Circumvallate placenta	Placenta previa
Bleeding prior to viability is not uncommon.	Bleeding more common after period of viability.
Bleeding usually slight and often accompanied by uterine contractions.	Bleeding often profuse, recurring and painless.
Seepage of amniotic fluid may occur.	No seepage of amniotic fluid.
Vaginal examination does not aid in the diagnosis.	Vaginal examination may disclose positive findings.
Roentgenologic examinations, including placentograms, do not reveal any abnormality.	Roentgenologic examinations, including placentograms, may disclose positive findings after the seventh month.

cumvallate placenta and placenta previa, and table 3 shows the distinguishing

TABLE 3

DIAGNOSTIC FEATURES OF CIRCUMVALLATE PLA-  
CENTA AND PREMATURE SEPARATION  
OF PLACENTA

Circumvallate placenta	Premature separation of placenta
Hemorrhage is evident.	Hemorrhage is commonly concealed.
Shock is not present.	Shock may be present.
Uterus relaxes between contractions.	Toxic uterine contractions
Toxemia is unusual.	Toxemia is relatively common.
Bleeding prior to viability is not uncommon.	Hemorrhage more likely to occur in course of period of viability.
	Evidence of fetal distress or death.

features of circumvallate placenta and abruptio placentae. In several instances, it was impossible to distinguish between partial premature separation of the placenta and circumvallate placenta until the placenta was inspected.

#### MANAGEMENT

Only scant comment can be made concerning the management of this condition because only a presumptive diagnosis can be made until the placenta can be inspected. In a case in which hydrorrhea gravidarum develops, an effort should be made to prevent infection by the daily instillation into the vagina of one of the newer nonirritating, liquid antiseptics.

The management of bleeding during pregnancy, in the absence of evidence which will permit a positive diagnosis of placenta previa or of abruptio placentae, is one of expectancy. This requires great patience on the part of both the patient and physician. The patient must remain in bed, perhaps for many weeks, and the physician must have the forbearance to defer operative methods of delivery, such as cesarean section, unless symptoms indicate that this method of delivery is urgent.

#### COMMENT

One or more of the following signs or symptoms were observed in 24 of 47 instances of circumvallate placenta: (1) signs of threatened, but not inevitable, abortion; in many instances these signs recurred or did not subside; (2) prolonged but seldom profuse vaginal bleeding; (3) intermittent uterine contractions, and (4) early rupture of the membranes with hydrorrhea followed eventually by premature labor, sometimes prior to the third trimester of pregnancy. If hydrorrhea is present, prognosis for the fetus is poor.

The maternal hazard is due to hemorrhage and potential infection. The hemorrhage is seldom profuse and no instance of death or even shock from hemorrhage occurred in the cases reported by Hobbs and Rollins.<sup>4</sup> Three patients in our series received blood transfusions; two of these also had placenta previa.

The danger of infection is potential because of the presence of blood in the lower part of the genital tract for a more or less prolonged period and because of the occasional (in ten instances of our series) prolonged period of time intervening between rupture of the membranes and labor. Postpartum fever occurred in two instances.

The fetal mortality was 24 per cent in the 47 instances of this anomaly. The anomaly was observed in 47 of 8,861 deliveries (1:188).

Repeated instances of circumvallate placenta in the same case have not been reported previously. We have observed five cases in which the anomaly occurred on more than one occasion. In four of these cases the anomaly was accompanied by symptoms of clinical importance. One of these patients had three deliveries each complicated by circumvallate placenta; all three babies survived, although two of them weighed only 1,270 and 1,360 gm. respectively. Two of the mothers, who each had this complication on two occasions, lost the infants prematurely. Almost all of the women who had a recurrence of circumvallate placenta had other pregnancies which were not complicated by this anomaly and a majority of the women who had only one pregnancy that was complicated by this anomaly had other uncomplicated pregnancies and gave birth to living children at full term. It is evident that there is a definite tendency toward the recurrence of circumvallate placenta which occurred nine times among four of the 19 patients who had clinical symptoms.

Circumvallate placenta is probably one of the few known etiologic factors in the condition known as hydrorrhea gravidarum, although it does not explain all instances of this condition, especially those in which the pregnancy proceeds to term. Circumvallate placenta is an obstetric entity of definite fetal and some maternal significance which should be kept in mind when one is confronted with unaccountable bleeding in the course of pregnancy. The frequency of the occurrence of circumvallate placenta and the fetal hazard of this condi-



tion are not generally appreciated. Conservative management of protracted slight bleeding or of hydrorrhea during pregnancy requires great patience on the part of the patient, her relatives and the physician. In a number of instances, patience has been rewarded by the survival of a prematurely born infant.

## DISCUSSION

Dr. J. S. Hebert (New Orleans): Dr. Mussey has given us a complete and most interesting paper on circumvallate placenta. Certainly I did not mean to say any more, except to thank him for such a valuable report. However, I would like to report a case in which two important points in his paper are brought out. First, severe hemorrhage does complicate the clinical course of a pregnancy to the extent of fatalities in babies. Second, the condition may be repeated.

In 1924 a first pregnancy resulted in a term spontaneous delivery of a normal healthy baby. In a second pregnancy, in 1926, resulted in a term spontaneous delivery of a normal healthy baby. In 1929 a third pregnancy resulted in a complete six weeks' spontaneous abortion. In 1930 a fourth pregnancy was normal until the eighth week, when bleeding started; the bleeding continued through the twenty-fourth week; patient remained more or less in bed these sixteen weeks. From then on to term the pregnancy ran a normal course and resulted in term spontaneous delivery. This fourth pregnancy furnished the complete circumvallate placenta reported by Dr. Deeves in 1930. Then in 1933, a fifth pregnancy resulted in a complete eight week spontaneous abortion. In 1936 a sixth pregnancy ran a normal course until the eighth or ninth week, when bleeding started. This bleeding ran through the fifteenth week, when it stopped. Bleeding then began again about the thirty-second week and was so severe that it resulted in a premature spontaneous delivery. This child did not live. This placenta, though not complete, was of the circumvallate formation. In 1939 a seventh pregnancy resulted in a term spontaneous delivery of a normal healthy child. In 1944, for the eighth pregnancy which had been referred to one of my confreres, bleeding started about the eighth week, the hemorrhage continued and became so severe that pregnancy was terminated about the twenty-fourth week. No report on placenta was made.

Dr. Beacham (New Orleans): I am sure that I express the opinion of everyone here when I state that we are very grateful to Dr. Mussey for taking his valuable time to make a trip to New Orleans to speak to us on this important subject. In the future we will be on the lookout for these cases, and I hope within the next few years we can report to him that we have achieved the de-

gree of accuracy of diagnosis which his group has attained.

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## CHRONIC PENUMONIAS\*

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NEW ORLEANS

Although bronchiectasis, atelectasis and lung abscess are well-recognized entities, chronic non-specific pneumonias have not been given as much attention in medical literature as their frequency warrants. These chronic pulmonary inflammations are distinguished from ordinary acute pneumonia by massive exudation into the alveoli<sup>1</sup> followed by organization, suppuration and fibrosis.

Such chronic pulmonary inflammations are marked by exacerbations of cough and expectoration, chills and fever, dyspnea and thoracic pain alternating with periods of relative freedom from symptoms. The onset may be explosively acute as in pneumococcal pneumonia or insidious with few systemic symptoms as in the series of cases reported by Rich and Hamman.<sup>2</sup> In their patients, all the pulmonary interstitial tissues were hyperplastic and the alveolar walls tremendously thickened. Connective tissue proliferation within the alveolar walls compressed the capillary circulation of the alveoli and (independent of alveolar exudate) lead to progressive pulmonary fibrosis, increased pressure in the pulmonary artery and to right ventricular hypertrophy with congestive heart failure as a terminal phenomenon.

At times a definite etiology can be established in these cases by obtaining from the

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sputum a pure culture of staphylococcus,<sup>5</sup> streptococcus or Friedlander's bacillus<sup>3</sup> or by postmortem isolation of an irritating lipid<sup>4</sup> from the lung. More often than not the exact cause is not determined because sputum studies are inconclusive, the flora apparently varying from day to day. Since the time of Laennec (1826) controversy has centered about these chronic pneumonias. Do they arise insidiously as chronic states or do they begin with acute phases? Often, one cannot answer this question satisfactorily.

The most impressive symptoms are dyspnea and bronchospasm so severe that very often the diagnosis of bronchial asthma is made, but the history is not the characteristic one of allergy. Rather it is one of repeated episodes of respiratory tract illnesses of varying severity. At times, it is difficult to eliminate congestive heart failure as the cause of symptoms. Differential venous pressures may be of assistance but frequently one must resort to a trial of digitalis which seldom helps these patients unless congestive heart failure has actually resulted from the massive pulmonary destruction. Generally this syndrome is established in middle life, and these patients are invariably "sickly" and underweight. Even in remission, there is pronounced lowering of respiratory reserve. Usually the roentgenogram indicates that the more centrally situated portions of the lung are consolidated and the more peripheral segments emphysematous. As Davison has pointed out, these cases do not fall clearly into the classification of bronchiectasis or lung abscess. A minor degree of bronchial damage<sup>8</sup> and bronchiectasis can be demonstrated by the pathologist postmortem or by the bronchoscopist antemortem, but the preponderant damage is to the lung parenchyme.

Not infrequently this syndrome results from organization of an unresolved pneumonia which apparently had begun as any other acute pneumonia. During ordinary bacterial pneumonia, a considerable amount of exudate is deposited in the alveoli; if it cannot be resolved by digestion and resorption, organization and fibrosis occur. Inas-

much as it can be produced experimentally either by leaving an excess of serum in the alveoli or by impeding lymphatic drainage, it is presumed that whatever blocks drainage (as by a mixed infection, pneumonia or by anthracosis<sup>6</sup>) may result in the analogous phenomenon clinically. Granulation tissue from various points on the alveolar walls gradually replaces the alveolar exudate and fills the alveoli with a contracted, dense, nearly airless mass of connective tissue. If there is additionally an empyema not speedily corrected, there will also occur shrinking and distortion of the hemithorax;<sup>7</sup> the trachea, heart and mediastinum are drawn to the affected side, the diaphragm is elevated, and the chest wall markedly retracted. This lessens the mobility of the entire thorax and greatly embarrasses respiration. When the antecedent pneumonia has been secondarily invaded by staphylococci or streptococci, multiple abscesses may honeycomb a lobe or even the entire lung and lead to further septic complications. At times cavities may be scattered among foci of organizing pneumonia.

It is highly probable that chronic pneumonia will some day be recognized as an industrial hazard. In certain industries, notably those involving work with lacquers and shellacs, there is exposure to irritating lipids.<sup>4</sup> These contain fatty acids which injure the lung, the degree of destruction being proportional to the speed of hydrolysis and the amount of free acid released.

Inasmuch as the outlook for these patients is not good, and the treatment at best is symptomatic, it is essential to eliminate chronic fibroid tuberculosis, lung abscess, bronchiogenic carcinoma, bronchiectasis and allergic bronchial asthma for all of which definitive therapy is at hand. For patients with chronic pneumonias, treatment must be designed to enhance the natural resistance and to improve pulmonary ventilation.

During the exacerbation, complete bed rest is essential. Since there are undoubtedly many fresh foci of acute inflammation superimposed on the chronic substrate, opportunity must be afforded for a maximal



resolution of these. Oxygen by tent is usually necessary and bronchodilating drugs are needed. If these do not suffice, bronchoscopy will be required to free the bronchial tree of tenacious mucus. Antibiotic and sulfonamides sometimes seem to benefit, especially when inhalational methods are employed. Blood transfusions are usually indicated for the almost invariably concomitant anemia.

During the periods of remission, every effort should be made to favor bronchial drainage. Ventilation is at times enhanced by shrinking the nasal mucosa, while bronchial dilation is effected by aminophylline, epinephrine or ephedrine. Postural drainage and even repeated bronchoscopies may be required. Thinning of the sputum by expectorant cough agents is desirable, but the use of opiates to depress the cough reflex is injurious. In several European clinics, irradiation of the lungs has been practiced, but the tabulated results are not particularly impressive. It is to be emphasized that nutrition is to be maintained despite the patient's natural aversion to eating. As far as is practicable, the patient must be encouraged to conserve his respiratory efforts.

The prognosis is obviously poor. These people may live many years but they are seldom free of symptoms entirely. The course is progressively downward as the acute respiratory tract episodes tend to become more frequent and more severe. With the use of the newer chemotherapeutic agents, it is possible that the progress of the disease may to a considerable degree be slowed.

#### SUMMARY

The clinician encounters chronic pulmonary inflammations more often than is generally appreciated. The etiology may sometimes be established by examination of the sputum, but more often it cannot. The syndrome is featured chiefly by cough, lowering of respiratory reserve, intense dyspnea and marked weakness. The course is usually one of progressive debility, at times terminating in congestive heart failure. Treatment is designed to improve the pa-

tient's nutrition, to increase respiratory function by bronchodilatation and to combat bronchial infection by chemotherapy.

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### DRUG REACTIONS AND THEIR TREATMENT, WITH SPECIAL REFERENCE TO THE USE OF BAL IN HEAVY METAL POISONING.\*

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AND

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NEW ORLEANS

Because of the abundance of material dealing with reactions to the newer drugs and because of the limited use of BAL in one practice, Dr. Henington and I have collaborated on this paper. Dr. Henington will present the reactions to benadryl and pyribenzamine, and I am covering the reactions to penicillin and the use of BAL in heavy metal poisoning.

It is not our purpose to detract from the unquestioned value of these drugs but merely to point out the limitations and,

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under some circumstances, the actual dangers of their use.

#### PENICILLIN

### I. Routes of administration:

- (1). Oral—
  - (a). Tablets (25,000 units)  
(50,000 units)  
(100,000 units)
- (2). Parenteral—
  - (a). Aqueous
  - (b). In beeswax and peanut oil
- (3). Topical applications—
  - (a). Aqueous
  - (b). In water soluble ointment bases
- (4). Inhalation—atomizer sprays
- (5). Constant intravenous drip
- (6). Intrathecal

### II. Reactions due to the drug itself:

- (1). Toxic erythema
  - (a). First to third day of treatment.
  - (a). Most often occurs after oral administration.
  - (c). Manifested by generalized diffuse, fine, red, macular rash with pronounced subjective symptoms of itching.
  - (d). Rash clears in seven to 10 days and is characterized by diffuse peeling.
- (2). Urticaria
  - (a). Occurs within seven to 14 days after exposure to drug.
  - (b). May follow all types of internal medication. The incidence of urticaria following the use of penicillin in beeswax and peanut oil is about 5 per cent,<sup>1</sup> no greater than that following aqueous solutions or oral medication. After beeswax and peanut oil injection, local reactions consisting of painful swelling and urticaria-like wheals surrounding the site of injection are quite common but of little consequence.
  - (c). The urticarias are slight to severe with angioneurotic

edema and sometimes with arthralgia.

Our findings are in accord with the conclusions of Pillsbury<sup>2</sup> and his associates, who report:

- (a). Reactions are more frequently encountered in patients who have had repeated courses of this drug.
- (b). The incidence of urticaria is increasing, being 1.8 per cent in 1944 and 5 per cent in 1946.
- (c). Readministration of the drug after severe urticarial reaction may or may not be followed by recurrence of the urticaria on reinjection of a full therapeutic dose of penicillin.
- (d). It is sometimes possible to continue penicillin therapy in a reacting patient by the simultaneous administration of an antihistamine drug.
- (e). Skin tests are unreliable.
- (f). Antihistamine drugs are particularly useful in controlling reactions.
- (3). The fungus dermatophytiid-like reactions
  - (a). Early in the course of the therapy.
  - (b). Patient who has had an "almost forgotten" Jock-strap itch which recurs during the injections of penicillin and clears up in a few days after medication has been discontinued.
  - (c). Vesicular "dermatophytiid" eruption of hands and feet characterized by deep seated blisters along the sides of the fingers and toes. This clears up within a few days after medication has been discontinued.
- (4). Reactions following topical use on the skin
  - (a). Often occurs in nurses.



- (b). Incidence of allergic reactions is high.
  - (c). Local reaction is typical of dermatitis venenata.
  - (d). Subsequent internal medication may flare up a previously sensitized skin area.
- (5). Intrathecal
- (a). Immediate reactions of headache and nausea.
  - (b). Convulsions occur usually in single doses of over 100,000 units.<sup>3, 4, 5</sup>
- (6). Reactions in syphilitic patients: The Herxheimer reaction and the therapeutic paradox
- (a). Early syphilis (primary, secondary, asymptomatic with history under two years).
    - (1). Herxheimer reaction occurs in 35 to 50 per cent of all cases.
      - (a). Manifested by fever, chills, malaise, accentuation or precipitation of secondary rash, edema, or relapse of primary.
      - (b). If fever occurs during penicillin therapy, syphilis should be suspected in that individual.
      - (c). Treatment should *never* be discontinued because of this.
  - (b). Congenital syphilis
    - (1). Fifty per cent have Herxheimer reactions which consist of sharp elevations in temperature which do not appear to be injurious to the child.<sup>6</sup>
    - (2). Fatalities have been reported in premature malnourished infants.<sup>7</sup>
- (3). Pediatricians are in general agreement that the gradual building up of the dosage is unnecessary in these cases.
- (c). Syphilis and pregnancy
- (1). Incidence of abortion is no higher during penicillin treatment of the mother than during other forms of anti-syphilitic treatment.
  - (2). Incidence of abortion is no higher than the expected incidence of abortion in normal women.<sup>8</sup>
- (d). Cardiac syphilis
- (1). Because of the always potent danger of a Herxheimer reaction in cardiovascular syphilis, it is felt that these cases should always either:
    - (a). Receive prolonged preliminary courses of bismuth (two months) and iodides, or
    - (b). Twenty-four injections of 5,000 units at three hour intervals followed by 180 injections at 50,000 units.
- (e). Central nervous system syphilis
- (1). Asymptomatic. Herxheimer reactions not of serious import.
  - (2). Acute syphilitic meningitis. Herxheimer reaction not of serious import.
  - (3). Paresis and tabes dorsalis with or without optic atrophy. That these cases require special care can best be

illustrated by the following cases:

#### CASE NO. 1

41 year old male with proved central nervous system syphilis manifested by blurred vision, optic atrophy, and an Argyll Robertson pupil, entered the hospital for combined penicillin and malarial therapy. Penicillin therapy was begun at the rate of 50,000 units every three hours. On the third day of this treatment he suffered the first tabetic crises of his career with girdle pain and band-like feeling of constriction around his upper chest. He had no bowel movement for three days and his abdomen was slightly distended. The crises passed and he was discharged at the end of ten days, having received a total of 8,000,000 units of penicillin.

Five days later he was again observed. He had developed a rolling gait, loss of voluntary bladder and anal sphincter control, a feeling of numbness of both great toes, and the girdle pains and feeling of constriction around his upper chest was constantly present.

Six days later, 21 days after the beginning of penicillin therapy, he re-entered the hospital with a marked increase in all his symptoms and complete inability to walk. The symptoms gradually subsided, sphincter control returned, and at the end of three months the patient was able to get about with the aid of braces and a cane.

It was felt that his symptoms occurring, as is commonly the case, in the first 48-72 hours were due to a Jarisch-Herxheimer reaction brought on by the use of penicillin.

#### CASE NO. 2

A 49 year old colored male with tabo-paresis and cardiac syphilis (aortic regurgitation) had symptoms of speech and muscular incoordination associated with optic atrophy. He was a cheerful, ambulatory, and privileged patient on the ward for the first twenty-one days of hospitalization. He was started on 10 drops of a saturated solution of potassium iodide on the fourteenth hospital day, and on the nineteenth hospital day he received 1 c.c. of bismuth subsalicylate intramuscularly. On the twenty-first hospital day he was started on penicillin at the rate of 80,000 units every three hours. Two days later he began a rapid mental deterioration, finally necessitating transfer to a mental institution.

Penicillin was not interrupted because we did not at that time think the change to be more than a transitory one. Now there seems to be reason to believe, both from our own experience and from the experience of others,<sup>9</sup> that Herxheimer reactions cause permanent damage. Tucker and Robinson,<sup>9</sup> of Baltimore, report some reactions to the initiation of treatment in 26 per cent of patients. It is impossible to prove that penicillin is the cause of the exacerbation of symptoms as the therapeutic para-

dox is a well-known fact in central nervous system syphilis.

It would seem wise, however, in cases of general paresis, tabes dorsalis, or progressive optic atrophy, to follow the method of treatment advocated by William A. Leifer.<sup>10</sup> He recommends twenty-four injections of 5,000 units at three hour intervals followed by 180 injections of 50,000 units, making a total dosage of 9,120,000 units.

#### BAL (BRITISH ANTI-LEWISITE)

During the last war a drug was developed to combat arsenical poisoning from lewisite.<sup>11</sup> It is known that arsenic forms a stable compound with—SH (sulfhydryl) groups in the body tissues preventing them from performing their proper functions. This drug, by virtue of being a dithiol, forms an inert stable compound with the arsenic permitting its removal from the tissues and rapid excretion by the kidneys.

Eagle<sup>12</sup> has made an extensive report of cases in which BAL has been used in complications of arsenical therapy. Sulzberger and Baer summarized his findings as follows:

- (a). Arsenical dermatitis: In 88 cases, 80 per cent responded to treatment.
- (b). Toxic encephalitis: In 55 patients, 44 recovered completely within one to seven days and 11 died.
- (c). Agranulocytosis: In 11 cases, 10 recovered with one death.
- (d). Aplastic anemia: In three cases, there was no beneficial effect from BAL.
- (e). Jaundice: In 14 patients, five showed prompt response, seven evidenced no effect, and in two the effects were debatable.
- (f). Massive overdosage of oxophenarsine hydrochloride: In four cases there were three with prompt improvement and one death.
- (g). Arsenical fever: There were 44 cases with prompt recovery in all.

Because gold and arsenic resemble each other clinically and behave similarly in the tissues, BAL was tried in the treatment of gold reactions and proved to be very effec-



tive. In a recent journal of the American Medical Association there was a report of marked improvement in six out of seven cases treated with this drug.<sup>13, 14</sup> Twenty-five out of 26 cases of acute mercury poisoning survived following treatment with BAL.<sup>15</sup>

In treatment of severe gold or arsenical poisoning, it is recommended that 3 mg. per kilogram of body weight of BAL, 10 per cent in oil, be given intramuscularly every four hours for the first few days, five injections on the third day, and two daily thereafter for ten days, or until recovery. In milder cases the dosage may be reduced to 2.5 mgm. per kilogram. In mercury poisoning the initial dosage is usually higher, 5 mgm. per kilogram followed in one or two hours by a dose of 2.5 mgm. per kilogram of body weight. Then as in arsenic poisoning.

Side effects include profound weakness, nausea, vomiting, headache, muscular aches, lacrimation, and salivation.

There follows three cases of arsenic poisoning treated with BAL:

#### CASE NO. 1

A 36 year old male entered the hospital in an extremely serious condition. He had a generalized exfoliative dermatitis associated with a marked toxemia. He had received seven injections of mapharsen in a period of 27 days for a total of 0.32 gm. The rash started after his fifth injection, was greatly aggravated by the sixth, and became generalized after the seventh. Twenty-seven days after his first symptoms appeared and 12 days after the condition had become generalized, he was given BAL at the rate of 2.5 c.c. of the 10 per cent solution in oil intramuscularly every four hours for a total of 10 injections. The drug was discontinued because of abscess formation at one of the sites of injection in his right buttock and because the patient, ambulatory on admission, had become so profoundly weak from the injections he could not turn over in bed. This side effect of the drug disappeared in the first 24 hours after the drug was discontinued. The response of the patient to the drug began with his first injection. The rash, edema, and toxemia all faded rapidly, and on the twelfth hospital day the patient was discharged with a mild residual dermatitis on his groins.

#### CASE NO. 2

A 27 year old colored male with early latent asymptomatic syphilis was given 60 mgm. of oxophenarsine hydrochloride and 200 mgm. of bismuth.

Three days later he received another 60 mgm. of oxophenarsine hydrochloride. On the evening of his second injection of arsenic, the patient complained of a severe headache and became stuporous and irrational. A diagnosis of hemorrhagic arsenical encephalitis was made and he was given 2 c.c. of a 10 per cent BAL in oil solution, through error, intravenously rather than intramuscularly. He immediately became cyanotic and dyspneic and appeared to be in shock. The blood pressure was 110/70, pulse rate 60 per minute, the eyes were dilated but reacted slowly to light. There was moderate nuchal rigidity present.

The patient was not given any treatment at this time and the next day was given 2 c.c. of BAL intramuscularly. He had improved tremendously over night and except for a slight clouding of his sensorium he was perfectly normal, being discharged on the fourth hospital day as perfectly recovered.

This case should give us some courage in the use of this new drug in that a patient survived an accidental intravenous injection of an oil solution.

#### CASE NO. 3

That BAL may be of use in chronic arsenical poisoning is best illustrated by the following case. A 45 year old colored female entered the hospital with a chronic generalized exfoliative dermatitis which had become exacerbated in 1937, 1938, and 1942, following her employment in spraying cotton with an arsenical. After three weeks without improvement, she was started on BAL at the rate of 1.5 c.c. of the 10 per cent solution in oil every four hours for two days and then 1.5 c.c. twice a day for five days, then 1 c.c. daily for eight days. On the eighth day she was discharged greatly improved. Her skin was smooth and itching had subsided. Fissuring and thickening of the palms and soles were the chief residue.

#### CONCLUSIONS

The reactions to penicillin are listed. Special attention has been called to the permanent aspect of the Herxheimer reaction in the treatment of late syphilis.

In BAL we have an extremely safe and valuable drug with which to combat arsenic, gold, and mercury poisoning.

#### REACTIONS TO BENADRYL AND PYRIBENZAMINE\*

The study of any new drug is often speculative, since neither the optimum dosage nor the diseases which should be treated, can be predicted. Furthermore,

\*This portion of the paper was presented by Dr. Henington.

side reactions might occur which had not heretofore been mentioned by other observers. Because the new "magic drugs" in general have yielded such disappointing results in most dermatologic problems, it is natural that searches for new specialized forms of management have been pursued with great intensity by the dermatologist. Some advances worthy of mention will be recorded here.

In view of the gradually accumulating evidence that some features of the allergic reaction may be associated with the liberation of histamine, investigation has been directed towards synthesizing compounds that might counteract certain pharmacologic effects of histamine. Several such substances have been studied within the past few years but because of their toxicity have proved unsuitable for clinical use. However, two of these substances have received favorable clinical trial and they have been named benadryl and pyribenzamine, respectively. It appears likely that in the future more compounds in this series will be discovered that may prove to have an even greater pharmacological activity.

Benadryl is a white crystalline powder which may possibly be slightly opalescent. It is soluble in water and alcohol and is stable under ordinary conditions of temperature and pressure. It has been administered orally, intramuscularly and intravenously, and is available in capsules of 25 and 50 mgm. and as an elixir with 10 mg. of benadryl in 4 c.c. (Z/i) of the mixture. The average adult dose is 50 mg., repeated three or four times a day, and the total daily dose has varied from 50 to 500 mg. The elixir in doses of 10 or 20 mgm. (one or two teaspoonfuls), repeated three or four times a day, may be given to children. A child's dose is usually derived by allowing 2 mg. of benadryl per pound body weight divided into two to four doses. The amount of drug required in both children and adults will vary with the severity of the allergic symptoms.

Study at the Mayo Clinic showed that benadryl: (1) decreases the cutaneous vasodilating action of histamine; (2) alle-

viates the nasal congestion induced by the vasodilatation of the mucous membrane caused by histamine; (3) may decrease the response of the gastric acids and the volume of gastric secretion provoked by the administration of histamine, and (4) depress the wheal and flare response in cases of hypersensitiveness to cold.

Benadryl is readily absorbed by all routes of administration and the maximum response following oral use is about 25 minutes, although it may be as rapid as 10 minutes. The therapeutic action usually lasts for five to eight hours.

No evidence is available to suggest a delayed or cumulative effect. Because drowsiness is encountered in a number of cases, it is well to avoid the concomitant use of sedatives and hypnotics. When the drowsiness is bothersome it may be counteracted in some cases by the simultaneous administration of ephedrine sulfate or benzedrine.

*Clinical Use—Urticaria:* Contis and Owens<sup>16</sup> prescribed benadryl for eighteen patients with various types of urticarial eruptions, and eleven patients had complete disappearance of the eruption during treatment. Four patients did not respond to the usual dosage of 50 to 100 mgm. given orally one to five times daily.

In treating cases of chronic urticaria, angioneurotic edema and dermatographia, when the drug was discontinued there was prompt recurrence of the disease. Of the first 52 cases treated by Todd,<sup>17</sup> 47 were completely relieved, four were partially relieved, and one was relieved of whealing, but not of pruritus.

From these experiences, it appears that benadryl is highly effective in the treatment of angioneurotic edema and urticaria when administered orally in 50 to 100 mgm. doses repeated two to six times a day. In the majority of cases relief is achieved only while the drug is being administered.

Urticaria occurring in serum sickness and following liver injections or penicillin therapy has also been controlled by the use of benadryl. In some instances the relief thus afforded allowed continued injections of the medication.



*Hay Fever and Vasomotor Rhinitis:*

Koelsche, Prickman and Caryer<sup>18</sup> treated 52 patients with hay fever and obtained over 50 per cent improvement in three-fourths of the cases. The dosage employed was 50 to 100 mgm. administered by mouth three times daily. These authors also showed that combining 3/8 gr. of ephedrine sulfate with the benadryl produced an increased amount of relief.

*Asthma:* Suffice it to say that benadryl has been disappointing in the treatment of asthma. Koelsche, Prickman and Caryer administered benadryl to twelve patients with bronchial asthma and only four reported relief. Of three cases reported by the Mayo Clinic, one was improved.

Benadryl has been prescribed in a variety of other unrelated conditions to achieve an antihistamine or an antispasmodic effect. Among these disorders are contact dermatitis, migraine, Ménière's syndrome, erythema multiforme and dysmenorrhea. Whether it will prove effective in these and in other conditions is not clear, and its effectiveness will undoubtedly be the subject of future studies.

*Reactions:* No skin eruptions or febrile disturbances have been reported following its use and it is not habit forming.

Clinical observations on the use of benadryl: All "serious reactions" to benadryl thus far reported have occurred in patients practicing self medication, who have substantially increased the dose prescribed by the physician. Borman reports the case of a Catholic nun who took 40 capsules of 50 mg. each in a period of 24 hours (2,000 mg.). She became disoriented, lethargic and confused. The drug was immediately discontinued when she consulted a physician, and she recovered completely in twenty-four hours. Geiger and his group<sup>19</sup> in the A. M. A. report a case of complete shock following a normal amount of benadryl, namely, 50 mg., three times a day. After the first day of treatment, the patient complained of palpitation, dimmed vision, malaise without drowsiness and heartburn with nausea. Following the next regularly scheduled dose of benadryl (making a total

of 350 mg.), the patient was found unconscious in bed, cold, pale and pulseless. The blood pressure could not be obtained. A solution of epinephrine 7½ min of a 1:1,000 was given subcutaneously, and all medication stopped. Within 30 minutes the pulse was palpable, though weak. In three hours the patient was completely normal, with no recollection of what had happened. Although up to this time no deaths have been reported from benadryl, it is reasonable to assume that a patient taking the drug and not having the advice of a physician might well take an over dose and continue it until death is produced.

## PYRIBENZAMINE

Pyribenzamine is a synthetic compound which manifests a pronounced capacity to prevent many of the pharmacologic actions of histamine. Pyribenzamine on a weight basis is approximately six to seven times more active than benadryl in preventing fatal histamine shock in guinea pigs. Other experimental work on animals indicates that its activities are similar to benadryl and that it has relatively low toxicity. Studies in animals and man receiving pyribenzamine over notable periods of time have failed to reveal any untoward effects or the development of any significant tolerance to the drug. The exact mode of action is unknown. The average adult oral dose of pyribenzamine is 50 mg., repeated four times daily, preferably after meals. The total in adults has varied from 50 to 600 mg. depending on the severity of the allergic symptoms. In children a dose of 10 to 25 mg. repeated three or four times daily may be effective. The drug is available in tablets of 25 to 50 mgm. and suppositories 50 and 100 mg. respectively.

There is a marked similarity between pyribenzamine and benadryl, therefore, their uses parallel one another. Arhesmon and Koepf<sup>23</sup> studied 277 patients treated with pyribenzamine and they noted that relief of symptoms occurred within 15 minutes and persisted for four to six hours after the ingestion of the drug. In some instances a total daily dose of as much as

1000 mg. was given without untoward effect.

The experience with hay fever and urticaria treated with pyribenzamine was very similar to the benadryl studies. Thus, of 140 patients afflicted with grass and ragweed hay fever, 85 per cent had relief of symptoms. Of 15 patients with acute urticaria, all but one were notably relieved of symptoms. There were 44 patients with chronic urticaria and of these, 63 per cent were improved after taking pyribenzamine. The results of treatment of bronchial asthma were not satisfactory, but 46 per cent noted definite relief of bronchial symptoms when ephedrine sulfate and pyribenzamine were administered together a more notable improvement was obtained.

*Side-Reactions:* Side reactions are common, but rarely serious and in many cases do not demand that pyribenzamine be discontinued. The larger the dose employed, the more frequent will be the side effects. Drowsiness, dizziness, faintness, nausea and vomiting are the more common undesired effects. In some instances nervousness, drying of the mouth, and palpitation may be experienced.

The "serious reactions" occasionally seen with the administration of benadryl have thus far not been seen with pyribenzamine, making it, therefore, a relative harmless drug, yet having many beneficial effects. It is worthy to note that occasionally a patient can take both pyribenzamine or benadryl the first time without any reaction, but if it becomes necessary a week or a month later for the patient to take the drug again he will become drowsy and have many of the side reactions that we have just mentioned. Occasionally the reactions will be so uncomfortable that the drug will have to be discontinued.

#### FURACIN

Furacin is a lemon-yellow crystalline compound, slightly soluble in water, in alcohol, propylene glycol, and is most soluble in carbowax; therefore, the ointment is manufactured in a carbowax base. Furacin is produced by synthesizing pentose sugar from oat hulls and bran; these are chemi-

cally dehydrated to furfural and to this is added the nitro and semicarbozone groups to form furacin.

For the present, furacin is offered only in the form of furacin soluble dressing, a preparation for topical application in the treatment of infected wounds and surface infections, and for the prevention of wound infection. It contains 0.2 per cent furacin in solution. The pH is between 5 and 7.

Furacin soluble dressing becomes almost liquid at body temperature. It dissolves in serous fluids, blood and pus, thus reaching all parts of wounds. It does not cake or otherwise interfere with wound drainage. Furacin soluble dressing is a 1-500 solution of furacin in a water soluble vehicle containing carbowax 1500 and propylene glycol.

*Indications:* Based on the clinical findings to date, furacin soluble dressing is suggested for local application in the following conditions:

1. Infected surface wounds, or for the prevention of infection.
2. Infections of third and fourth degree burns.
3. Carbuncles and abscesses after surgical intervention, where conditions permit this therapeutic agent to reach the entire infected area.
4. Infected varicose ulcers.
5. Superficial ulcers of diabetics.
6. Secondary infections of eczema.
7. Impetigo of infants and adults.
8. Treatment of graft sites preparatory to skin grafting, and later to prevent infection.
9. Osteomyelitis associated with compound fractures.
10. Secondary infections of dermatophytoses.
11. The work of John Downing and his associates have also found furacin soluble dressing to be of beneficial effect in the treatment of many dermatoses, namely: infectious eczematoid dermatitis, erythema, sycosis vulgaris, dermatitis venenata with secondary infection, acne vulgaris, and diabetic and hypostatic ulcers.



Furacin's antibacterial spectrum includes both gram-positive and gram-negative organisms.

*Methods of Applying Furacin Soluble Dressing:* Surgeons now using furacin soluble dressing are applying it in various ways. It may be spread on gauze which is then laid over the wound and held in place by bandages, or applied directly to the affected area without bandaging. Moderate amounts may be placed in deep wounds and cavities and covered with a dry dressing. Furacin soluble dressing may be melted and poured over the wound. Some physicians advocate changing dressings one to three times every 24 hours. I usually suggest more frequent changing of dressings in weeping lesions, whereas in dry, inflammatory dermatoses one change every 12 hours is usually all that is required. For examination of wounds, the dressing may be rapidly and completely removed by irrigation with water or saline.

Drainage of pus pockets, removal of foreign and necrotic material and sequestra should always precede application of the dressing.

For skin grafts, furacin soluble dressing is applied both to the denuded area to combat infection and facilitate granulations and to the donor area to prevent infection.

*Reactions to Furacin Soluble Dressing:* Both the low toxicity of furacin and its low concentration (0.2 per cent) in furacin soluble dressing make highly improbable the possibility of producing systemic toxic effects from local application. Sensitization phenomena both locally at the site of the application of furacin and areas removed from the local site have been reported<sup>24</sup> and have been seen occasionally by us. Most reactions have occurred in patients who have been treated with furacin over a long period of time, that is a month or more. Previously eczematized areas are more likely to react to the drug than are new and clean wounds. The reactions thus far have not been serious although occasionally they

have been of a generalized eczematoid type and have lasted for a week or two. Sensitization is thought to be due either to the carbowax or the propylene glycol and not the furacin *per se*: work is being done now by the manufacturer to eliminate the sensitization properties of furacin soluble dressing.

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## THE CHEMOTHERAPY OF LEPROSY\*

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NEW ORLEANS

## INTRODUCTION

This paper was written with the intent of reviewing some of the attempts made to find a drug or drugs useful in the cure of leprosy. The material first suggested itself as suitable for a thesis subject and I first became interested in it after having talked with Dr. R. M. Wilson at Christmas, 1945, just before his return to Korea to take charge of the leprosy work in the United States Zone of that country. In the spring of 1946, my interest was firmly aroused upon hearing of the sulfone drugs then being used at the National Leprosarium in Carville, Louisiana.

The following material was gathered from reports in the literature and conversations with a number of leprologists—Drs. Wilson, McCoy, Faget, Johansen, Fite, Wolcott and Kellersberger; also, the photographs and exhibits in the laboratory at the Carville Leprosarium, demonstrated by Sister Hilary Ross, served to emphasize the treatment results.

In the discussion of the subject, I have taken the liberty to precede the actual drug therapy of leprosy with some more general remarks on the disease and its general treatment. Also, I have introduced the discussion of the individual drugs tried in the fight against leprosy with some statements of Muir on the evaluation of such drugs. Some of the substances represented in the literature by only one article have been excluded. Several physical agents which have been used from time to time in the treatment of leprosy, such as ultraviolet irradiation, x-ray irradiation, and the use of the Kettering hypertherm, have likewise been excluded. Incidentally, they have not been found of antileprotic value. Surgical excision of early lesions is also not discussed,

though it has been successful in several instances.

## GENERAL INFORMATION

*History, Geographic Distribution and Prevalence:* Leprosy has been talked about and described in writing since antiquity. Herodotus, the Cappadocian, in the Second Century, A. D., gave the first clear-cut picture of the disease. Since then such descriptions have not been lacking. The leper was dreaded in ancient times for his loathsome appearance (if he were in the advanced stages of the disease), and the fear of the supposedly extreme contagiousness of leprosy made its sufferer an outcast from men's society. This attitude toward the leper still prevails in large measure, and therefore, the sociologic aspects of the disease are of great importance.

Leprosy has been endemic in China, India, and the Nile Valley for many hundreds of years before the birth of Christ. In 480 B. C., the Persians brought it to Greece, and in 62 B. C., the Romans introduced leprosy in Europe. Segregation of lepers was practiced as early as 1500 B. C. by the Babylonians. During the sixth and seventh centuries the disease appeared in northern Europe, and it spread widely in the time of the Crusades. In the Middle Ages it slowly decreased in frequency in Europe and is now rare. In India, China, Japan, the East Indies, Philippines, Middle East, and Africa, it is still common.

How and when leprosy reached the New World—whether by white European settlers or from the negro slaves brought over from Africa, is not clear. There are now some 30,000 lepers in the Western Hemisphere.

In the United States, 385 lepers are now being treated at the National Leprosarium in Carville, Louisiana. Some 1,000 to 2,000 others probably dwell in the United States, many of them hiding the disease; others still undiagnosed. Most of the lepers in the United States come from Louisiana, Texas, Florida, and to a lesser degree, California.

It is estimated that there are three million lepers in the world today. Of these, according to Muir, one million live in India,

\*Awarded the Walter Reed Memorial Medal for the best thesis on a subject having to do with tropical or preventive medicine presented to Tulane Medical School.



another million in China, a half million in Africa. About 10 per cent of all lepers are under some sort of medical surveillance.

**Etiology:** A. Armauer Hansen, working in Bergen, Norway, in 1874, first saw an acid-fast bacillus which was very numerous in leprous tissues and he considered it the etiologic agent of the disease. The bacillus has since been named *Mycobacterium leprae*. Though known for over 70 years, this bacillus has never been satisfactorily cultured. That is, no one has been able to reproduce the results of those who claim to have cultured it, nor have animal inoculations been successful. In experimental work, therefore, it has been necessary to use rat leprosy, with the assumption that the bacillus of rat leprosy, *M. leprae murium*, has similar characteristics to *M. leprae*. Tuberculosis has also been used in the comparative analysis of various antileprotic drugs.

**Epidemiology:** Because the incidence is twice as great in men as in women, it has been thought that women are more immune to leprosy than men. Hopkins believed that negroes in Louisiana were more immune than white people.

The disease usually begins in childhood, adolescence, or early adult life. Rogers emphasized and showed statistically that 80 per cent of lepers come from homes in which a leprous person has resided for a long period of life. He reiterated the view that leprosy is a disease transmitted through long, intimate association with a leper, especially during the childhood years. The average age of admission, in one large series, to a leper hospital was 16 to 20 years.

All leprologists agree that the disease is only feebly contagious. The public's fear of leprosy is unfounded, for a casual contact with a leper is hardly conducive to infection. Rather, it is the long, intimate home association that spreads the disease.

In the United States, only the states bordering the Gulf of Mexico have repeatedly new cases of leprosy. In Minnesota, for instance, 200 Norwegian lepers settled in the latter half of the Nineteenth Century, yet the disease died out. On the other hand, new cases continue to crop out in Louisiana,

Texas and Florida. Perhaps the difference in climate is a determining factor in this problem.

**Symptomatology:** After an incubation period of one to 10 years or more, the disease begins to manifest itself. Rogers showed that in four-fifths of patients, the incubation period was less than five years.

Leprosy is classically divided into two types: nodular (lepromatous) and nerve (maculo-anaesthetic) leprosy. In cooler climates, two-thirds of the cases are nodular, while in tropical regions about two-thirds are of the nerve type.

Nodular leprosy begins with an outbreak of brownish-red macules which thicken and become pigmented. There is often associated irregular fever. The most common sites of eruption are the ear lobes, nasal alae, forehead, eyebrows, cheeks and skin. The eyebrows fall out. The nodules come and go and slowly spread and thicken. The skin of the entire face becomes greatly thickened, first hyper-, later anesthetic. The spots do not sweat. Folds are formed, and the thickened, wrinkled face is aptly described as "leonine." Eye involvement (conjunctivitis and iridocyclitis) is frequent, and blindness often results. Ulceration of the lesions is frequent. The patient finally, after several years, becomes cachectic, and somnolence precedes death.

Nerve leprosy results from the irritation of the granulomatous tissue surrounding peripheral nerves (especially the ulnar, anterior tibial, peroneal and facial nerves) with resulting neuralgia and paresthesia, finally anesthesia of the tissue supplied by the nerve. Anesthetic spots on the covered portions of the skin are pale, have an erythematous border. The skin becomes atrophic in these areas. Nerve trunks enlarge, especially the ulnar. First they are tender, later painless. Because peripheral anesthesia occurs, trophic changes and traumatic lesions of the toes and fingers give rise to absorption of the phalanges and large, non-healing ulcers on the exposed portions of the hands and feet. Contractures of the fingers and muscular palsies and

atrophies also result from the nerve atrophy.

The mixed type, seen frequently, is a combination of the nodular and nerve type.

*Pathology:* Granulomata containing swollen, bacilli-filled, pale-staining cells (globi) are found. These occur in the skin and subcutaneous tissue. In acute "lepra fever" episodes the bacilli may be recovered from the blood. In nerve leprosy the peripheral nerves are swollen. Cellular proliferations in the region of the blood vessels, later in the perineurium and finally the endoneurium compress the axis-cylinder with consequent degeneration.

*Diagnosis:* Aside from the identification of the signs and symptoms of leprosy, the most important procedure used in the diagnosis of leprosy is the recovery of the bacilli from a skin or mucous membrane (for example, nasal) smear or biopsy.

*Prognosis:* On the whole, the prognosis is unfavorable. Although spontaneous improvements occur at intervals, relapses usually follow. The nodular type runs a more progressive course than the nerve type. Patients with nerve leprosy may live 20 to 40 years. Tuberculosis and nephritis are the two complications which may carry the leper off within a few years of the onset of his illness.

*Prophylaxis:* Since the beginning of recorded medical history, segregation has been the chief tool in the leprosy control program. In past centuries, this segregation was so intense that the leper could not associate with any non-leprous person. He was treated worse than a criminal and deprived of all civic rights. In the Middle Ages, special hospitals in Europe were built to care for the lepers, and since that time segregation in special institutions has been the most common usage.

Rogers pointed out that compulsory segregation had failed wherever it had been tried, for the lepers were afraid of being "incarcerated" in a hospital and therefore hid themselves. The result of this concealment of the disease was a further spread and often advancement of the leprosy in these people to a hopeless degree, before

they were finally found and brought in for treatment. Rogers believed that for the vast majority of the world's lepers the most feasible, efficient, and economical method is a voluntary system to supply the most up-to-date treatment for early cases at clinics, and for more advanced ones in leper colonies with land to cultivate to supply most of their food and afford exercise for the patients.

Rogers<sup>1</sup> has stated: "For the rapid reduction of leprosy incidence, it is essential to adopt my plan of examining the households and other close contacts of all known infective lepers at not less than 6-monthly intervals for at least 5 years, with early treatment of the early cases thus detected." This plan proved successful on Nauru Island over a period of three years, with a reduction of the leprosy prevalence by 40 per cent.

It is essential to separate newborn children born of leprous parents from their parents immediately after birth. Special "healthy children" institutions have been evolved to take care of such children.

*General Treatment:* Patients must not only receive therapy with the drug in vogue, but they must also have supportive treatment. This supportive treatment is of great import in leprosy, since the disease is so long-lasting. Also, it is imperative to diagnose and eliminate any other diseases from which the patient happens to be suffering.

Non-specific treatment of local manifestations of leprosy must also be considered: Ulcers, especially on the legs and feet, have been treated with urea crystals applied locally daily, to hasten the extrusion of necrotic tissue and bone. In the Carville Leprosarium, streptomycin filtrate wet applications have been found to be effective. Nerve pains can be controlled with novocaine stellate ganglion or lumbar sympathetic block. Muir<sup>2</sup> advocates ephedrine given orally in capsules  $\frac{3}{4}$  to 2 gr.

Lepa reactions have been variously handled: Large doses of alkalis (sodium bicarbonate) have been tried to counteract the acidosis. Empirically, fuadin, 5 gm.



## SPECIFIC ANTILEPROTIC DRUGS

given intramuscularly, will often stop the severe fever in one to two days.

A diet well-stocked with proteins, carbohydrates, fats, and vitamins is necessary to make up for the weight loss and malnutrition so commonly seen in the lepers, especially in tropical countries. Also optimum nutritional state of the body helps to combat the wasting process resulting from the disease itself. Fresh meat, vegetables, fruit, and dairy products play a large role in the dietary regime. Dr. Basler, who has been in charge of a large leper colony in Nigeria for 10 years, told in a personal conversation how this dietary improvement alone produced a remarkable remission of the disease in many patients he has had under his care.

Lepers are often very despondent for they come to feel keenly their separation from even their dearest family members forced upon them by the rest of society. They may thus feel useless, even become sullen. Therefore, it is of importance to give them something to do while they live for prolonged periods of time with their fellow-lepers under institutional care. Vocational therapy, recreation facilities, religious services—all these play a large part in the treatment of leprosy. In regard to vocational therapy, the work often consists of dairy or truck farming, small "craft shop" goods manufacture, housework (cooking, sewing, and so on) for women. Recreational facilities can be developed with a band or orchestra, theatrical performances, glee club, games of both physical exertion and mental concentration varieties. Self-government of the patients has proved very popular at Carville, Louisiana. School for children and lectures for adults, are other things to be considered in this program. Provision of religious instruction and worship also must not be forgotten.

When the disease becomes "arrested,"—lesions becoming stationary and disappearing, and general health becoming robust—the patients are usually discharged from institutional care but are biannually examined for any recurrences.

*The Evaluation of Antileprotic Drugs:*

When reading about various drugs and their effects on leprosy, one is impressed by the glaring discrepancies of results obtained by different investigators using the same methods. Several important points, according to Muir, should be stressed in the judgment of the efficacy of drugs. The application of evaluation to chaulmoogra oil and its derivatives can be used as an example of the evaluation of the other drugs.

The first factor is the difficulty of classification of leprosy. The nodular type has the worst prognosis, the tuberculoid variety of nerve leprosy (of the Cairo classification) the best, with frequent spontaneous recoveries. Thus, spectacular cures of "nodular leprosy" may really have been tuberculoid patients who spontaneously recovered.

In the second place, there is a distinct difference between the incidence of the more severe nodular leprosy and the milder nerve leprosy in the tropics and in temperate climates. Most people have a high resistance to leprosy; only a small minority is easily infected. In temperate regions where leprosy is endemic and people live "hygienic" lives, only those with a low resistance will be sufficiently exposed to the disease to contract it. However, in the tropics, where people live crowded together, eat poor diets, live under conditions of filth and squalor, a much greater percentage of the population is exposed to leprosy than in temperate regions. Therefore, the milder nerve leprosy is more common proportionately, although the total number of cases is great. Because, then, the few cases treated in temperate regions are "nodular," therapy results are poorer than in the tropics, where most of the patients treated have the milder "nerve" type of leprosy.

No one has yet carried out a proper test for the efficacy of chaulmoogra oil in leprosy. For such a test, Muir stresses the use of the Lepromine test, which should be negative (indicating lack of resistance to leprosy) for six months before treatment, plus clinical and bacteriologic evidence of

activity. Secondary infections must be ruled out. Control cases should be treated with a bland injection of a similar substance,—olive oil, in the case of chaulmoogra treatment. Such a program must be carried on at least two years, a difficult project at best.

McCoy,<sup>3</sup> in summing up his views on the value of chaulmoogra, wrote in 1942: "My own observations have led me to the conclusion that the oil and its derivatives are of little or no curative value, and that the unpleasant side effects probably outweigh any advantage to the patient that may accrue from their use." Dr. McCoy, in a personal conversation, recently stated that he could find no use for the chaulmoogra derivatives in leprosy treatments.

The requirements for an ideal antileprotic drug, according to Muir, are: (1) It must be of sufficiently low toxicity so that, at least after the early stages of treatment, it can be safely administered without requiring elaborate tests, requiring considerable skill and time, and can be tolerated over a sufficiently long period of time; (2) it should be easy to administer and capable of being given by mouth; (3) it must be able to bring about steady improvement in the average case until the disease entirely disappears, and to prevent relapse; (4) it should be easy to manufacture and therefore capable of being produced at low cost in large quantities.

*Chaulmoogra Oil and its Derivatives: Source and Properties:* Chaulmoogra oil is obtained from the seeds of several trees found in the family *Flacourtaceae*, in particular from *Taraktogenus kurzii*, a tree found in Assam and Burma, *Hydnocarpus wightiana*, which grows in southern India and *H. anthelmintica* in Malaya and Indo-China. The oil of *Gynocardia odorata* does not contain the same fatty acids. The oil contains two unsaturated fatty acids with a closed ring consisting of five carbon atoms, a structure peculiar to this series of oils. The *Hydnocarpus* trees have been grown in Africa and South America to provide chaulmoogra oil for the local treatment of lepers.

In ancient China and India, chaulmoogra oil was used in the treatment of leprosy. In

the Chinese medical book, *Pen Tsao Kang Mu*, written about the fourteenth century, the following prescription is given: "Take 3 catties of the seeds, remove the hulls and grind to a fine powder. Discard those that have turned yellow. Pack in an earthen jar and seal tightly. Put the jar into a pot of boiling water and seal the pot so that no steam escapes. Boil until oil assumes a black and tarry appearance. It is administered in the following way:

Sophora flavescens	3 ounces
Chaulmoogra oil	1 ounce

Mix into a paste with wine and make into pills the size of the stersulia seed. Take 50 pills with hot wine before meals."<sup>4</sup>

A good description of the current native practices in prescribing chaulmoogra oil at the time and the properties of this substance is given in Watt's *Dictionary of the Economic Products of India*, 1890: "Chaulmoogra oil has long been known and used in the East as a cure for leprosy. In native practice of the present day the seeds and oil (of *Taraktogenus kurzii*) and of the closely-allied *Hydnocarpus wightiana* are both largely employed and are as a rule administered with "ghi" (clarified butter). As sold in the bazaars, the oil is commonly impure. The expressed oil is clear and of a pale sherry color and possesses a characteristic colour and odour. On being kept for some time it throws down a granular fatty deposit. Of late years the knowledge and use of the drug have spread to Europe, where it appears to be increasing in favour and reputation. The reputations of the drug most in repute in Europe are the pure oil and gynocardic acid, which is supposed to be the active constituent.

"Oil of *H. wightiana* is of a sherry yellow colour and devoid of the characteristic taste and odour of that of *T. kurzii*. Unlike the latter, which it otherwise closely resembles, it does not at ordinary temperatures deposit a crystalline fatty acid. It is chiefly employed as a lamp oil in Goa. The medicinal properties of this oil were neglected by Europeans until recently when they began to substitute it for the more expensive oil of *T. kurzii*. The oil must be used with a



certain degree of caution, as in certain cases it acts as a gastrointestinal irritant and produces vomiting and purging.”<sup>5</sup>

Monat, the first European physician to use chaulmoogra oil, in 1854 administered it in the form of the powdered seeds. Dr. Paul, Professor of Surgery at Madras Medical College, wrote in 1857: “In 1855 the therapeutic virtues of the Hydnocotyle and Choul Moogre received a fair trial at the hands of Dr. Porteous, and they were found to produce no amelioration.”<sup>6</sup> Dr. Bhan Daji reported several cures of leprosy with chaulmoogra oil in 1870. He charged such exorbitant prices that when the people who flocked to him found out he was but reviving the use of chaulmoogra oil, long known in India, his fame was short-lived.<sup>7</sup>

*Mode of Action:* The mode of action of chaulmoogra oil in the therapy of leprosy has been speculated upon by numerous investigators. In 1903, Talwik wrote that the oral administration of the drug produced leukocytosis, and the leukocytes destroyed the leprosy bacilli. Williams and Forsyth,<sup>8</sup> in 1909, concluded that “substances containing unsaturated fatty acids (e. g. cod liver oil, chaulmoogra oil) have the power of disintegrating the waxy envelope which surrounds the tubercle bacilli.” Mercado, in 1915, was of the opinion that the therapeutic effect was due to the phagocytic action induced by the leukocytosis. In 1920 Rogers reiterated the views of Williams and Forsythe. Because he thought any unsaturated fatty acids would have the same bacteria capsule-dissolving properties as chaulmoogra oil, he therefore used the less irritating cod liver oil (sodium morrhuate) and Soya bean oil.

In the same year McDonald and Dean at the University of Hawaii and Walker and Sweeney concluded from the “bactericidal action” of the chaulmoogra oil on rat leprosy bacilli and other acid-fast organisms, an action not seen in other fatty acids, that the chaulmoogra series fatty acids were active against those bacilli on account of their unique molecular structure,—a 5-cyclic carbon ring. Walker and Sweeney considered three possibilities as to the mode

of action of the oil: (1) It could have a direct bactericidal effect on *M. leprae*; (2) it could act indirectly by stimulating the tissues to react against the bacillus; (3) it may be inactive and improvement occur spontaneously. “An hypothesis which seems best to explain the mechanism of the bactericidal action of the chaulmoogra acids and their specificity for acid-fast bacilli is that these fat-elaborating bacilli attempt to utilize the chaulmoogra acids to build up their fatty capsules, and that these cyclic fatty acids contain a group or an arrangement of atoms which is toxic for the bacterial cell.”<sup>9</sup> Schobl, in 1923, also considered the action of chaulmoogrates to be due to their specific X-carbon cycle structure. Leukocytosis brings about the contact of the drug with the bacilli, according to Read, 1925.

In 1931 Muir wrote: “An important point for consideration is the manner in which hydnocarpus oil and its preparations act when injected into the tissues of the body. When injected into lesions by the intradermal method, there seems to be little doubt that a large part of the action is due to the local irritation set up, and that this irritative effect continues for a considerable time, the esters remaining unabsorbed inside the local cells. This results in breaking down and phagocytosis of the lepromatous material. Again, there is reason to suppose that the material set free locally may have an antigenic effect and result in the formation of antibodies which have a beneficial effect both locally and in other parts of the body. Both the injections given into the lesions and those given intramuscularly at a distance from the lesions probably act to a large extent by producing an effect analogous to protein shock; and it has been shown that protein shock produced by other methods, such as intravenous injection of dead bacteria, is distinctly beneficial in clearing up leprosy lesions.”<sup>10, 11</sup>

Lara and Lagrosa injected a small series of patients with the ethyl esters of chaulmoogra oil intramuscularly and in addition gave intradermal chaulmoograte injections on one side of the body and intradermal in-

jections of other vegetable oils on the other. They concluded that the chaulmoogra esters cleared up lesions on "their" side of the patient's body, while the other oils did not. However, they admitted that the series (14 patients) was too small to be definitely significant.

In the 1930's a group of pharmacologists at the University of California led by Emerson, Anderson, and Leake investigated the action of numerous drugs used against leprosy on rat leprosy, other acid-fast bacilli and on leprosy patients. From their extensive studies they concluded that the chaulmoogrates had a specific though not very pronounced effect on the disease, mediated through the unsaturation of the fatty acids, their optical activity, and their basic structure, the pentacycle group. Three agents survived this investigation: ethyl chaulmoograte, chaulphosphate, and a non-chaulmoograte, merthiolate. The ethyl chaulmoograte had a lower toxicity and was less irritating in animals than the other derivatives. Its therapeutic index was found to be higher than that of the other oil-soluble fatty acid derivatives. Its disadvantage consisted in its very slow systemic absorption, though it cleared local lesions. Because of this disadvantage of the ester, these authors developed a water-soluble derivative, to be administered intravenously,—dichaulmoogryl-betaglycero-phosphate, called chaulphosphate for short. It did not show the untoward side effects seen in other water soluble intravenously administered derivatives, namely hemolysis and venous sclerosis.

As previously mentioned, McCoy<sup>3</sup> considers the chaulmoogra drugs to have little or no therapeutic effect in leprosy.

It is now in order to consider the various chaulmoogra preparations, their manner of administration, advantages, disadvantages, and effects.

*Chaulmoogra Oil*: The oil itself, as found in the unprocessed seeds, was used in India and China in ancient times. It was found that if the seeds themselves were eaten, little or no nausea resulted, while the oral administration of the expressed oil was

fraught with gastrointestinal tract complications. Hopkins, in 1916, reported on the oral administration of chaulmoogra oil. He recorded 48 per cent of his patients as "improved," 17 per cent as "cured."

Cochrane<sup>12, 13</sup> sums up well the oral therapy: "Prior to the advances in purifying the oil, it was only possible to give it by mouth. If a patient is able to tolerate large doses by the mouth the disease will undoubtedly improve. Unfortunately, one cannot give, as a rule, large enough quantities to produce permanent results. The method of administration is to commence with 1 or 2 mm. in milk or other suitable vehicle, or the drug can be placed in gelatin capsules and given directly after meals. The dose is first given once a day, then increased to three times a day. Every other day the dose is increased by 2 mm. until about 100 mm. three times a day is reached. Seldom, however, can such large doses be tolerated, firstly because of the vomiting that the drug produces, and secondly because in large doses there is a tendency for toxic symptoms to appear, such as languor and emaciation. If the dose is persisted in when signs of intolerance have appeared there are dangers of fatty degeneration setting in."

Crude chaulmoogra oil has also been given by hypodermic injection. Tortoulis Bey, in Egypt, had a patient in 1894 who had severe vomiting after the oral therapy, and therefore had only been treated sporadically for a period of three years. Bey, therefore, injected the drug subcutaneously for a prolonged period of time, four years. The man's advanced lesions slowly healed. The disadvantages of injections of the crude oil are that there is marked local irritation, and the great viscosity of the oil makes it hard to inject.

*Heiser-Mercado Mixture*: In the Philippines, 1910, Seiser and Mercado brought out their "mixture", designed to be less irritating when injected subcutaneously than the crude chaulmoogra oil. The mixture was made up of 60 c.c. of camphorated chaulmoogra and olive oil with 4 gm. of resorcin. Even with this mixture, pain after intramuscular injection was common.



*Gynocardic Acid and Gynocardates*: Moss, in 1879, isolated a crystalline fatty acid with a melting point of 30° C. from commercial chaulmoogra oil. This substance he called "gynocardic acid", because he mistakenly thought chaulmoogra oil was obtained from *Gynocardia odorata*. Cottle reported on its oral use; Roux, in Paris, used it in 1891. In the same year Merck and Company prepared commercial gynocardic acid. In 1904 Power produced the salts, sodium gynocardate and sodium chaulmoograte.

It remained for Sir Leonard Rogers to popularize the chaulmoograte salts. He used a 3 per cent solution of sodium hydnocarpate. It was so irritating when injected subcutaneously or intramuscularly that it had to be administered intravenously. The disadvantages in this manner of injection were resulting thrombosis and phlebitis of the veins, a frequent occurrence. Also, there were occasionally severe fever reactions. The advantage, on the other hand, was easy injection, for the salt had a low viscosity and flowed well through the needle. Rogers then changed his injections to the sodium salt of the low melting point fatty acids found in chaulmoogra oil. This, in 3 per cent solution, he called "alepol." This material was given twice weekly, beginning with 0.5 c.c. and increased by 0.5 c.c. weekly up to 5.0 c.c. or more. Alepol has been used extensively in India by Rogers and his fellow workers and students. Certain economic advantages of alepol over other chaulmoogra products exist: It is packed as a powder for shipping and is therefore cheap to transport. The drug itself is cheap. Also, 1 per cent novocaine can be added to make injections painless.

*Ethyl Esters of Chaulmoogrates*: The ethyl esters of the acids in chaulmoogra oil have been the most widely used chaulmoogric substances in the last two decades, and they were recommended as the "most efficacious" agents in the treatment of leprosy at the Cairo Leprosy Conference in 1938. However, the Congress emphasized that chaulmoogra treatment should be suspended during a lepra reaction. One advantage the esters have over the plain chaulmoogra oil

is that they are liquid at all ordinary temperatures, while the oil itself must be heated before injection to overcome its great viscosity.

The esters were first produced in 1904 by Power. However, it was Engel Bey,<sup>14</sup> in Cairo, who wrote to Bayer and Company of Elberfeld, Germany, in 1909, with the request "to see whether they could not obtain a pure preparation of the active principle of the oil or at least a purified article free from the injurious effects of the ordinary oil." The Bayer Company chemists produced the ethyl esters of the total fatty acids found in chaulmoogra oil and called the product "Antileprol." This substance was injected intramuscularly and found to be much less irritating than the purified chaulmoogra oil. Bey initially also gave it orally to some of his patients and noted that gastritis did not occur. The oral dose used was 2 to 5 gm. per day, beginning with 0.5 gm. Since then, it and the other ethyl esters have only been given parenterally.

In 1917, McDonald and Dean<sup>15, 16</sup> and Hollman,<sup>17</sup> in Hawaii, began their work on the ethyl esters of fractions of the fatty acids of the chaulmoogra series. In 1920, they reported the successful use of mixed ethyl esters of the total fatty acids of chaulmoogra oil, administered intramuscularly, with the addition of 2 per cent iodine to decrease the irritative qualities of the chaulmoogra. The drug was given in the gluteal muscles once or twice a week, beginning with 1 c.c. doses, later increased to 5 or 6 c.c. After two years of treatment, they discharged 48 out of 186 treated patients as "arrested." In a report in 1922, Hollman tabulated 84 discharged patients and wrote that 60 were tuberculoid and 24 anesthetic. If this classification is the same as that now used, then one could expect to have a number of spontaneous recoveries from true tuberculoid leprosy, and the anesthetic type is also less severe than the nodular variety of which Hollman says nothing. On the other hand, if tuberculoid in his report

means true nodular leprosy, then these arrests of the disease are of significance.

Moogrol, a commercial preparation of very similar nature and sold by Burroughs Wellcome and Company, has also been widely used.

The most numerous articles on the use of chaulmoogra ethyl esters have come from the large Culion Leper Colony in the Philippines. There, four to five thousand patients have been constantly under treatment, and thus these reports have usually dealt with fairly large numbers of patients. At Culion, the Dean ethyl esters were primarily used in the 1920's and 1930's, with the addition of 0.5 per cent iodine, this mixture having been found to be the least irritating. Lara, however, thinks iodine has some other manner of producing its beneficial action. Not only were the esters given intramuscularly (and subcutaneously near lesions), but intradermally at the site of leprosy lesions. This intradermal injection technic was also called the "plancha" or infiltration method: 0.5 to 5.0 c.c. of the esters are injected, given in small amounts over the areas of the lesions, 5 to 10 mm. apart. The areas may not be reinjected until one month later, or sloughing will result, since it has been shown that the fat globules will remain in the local cells for several months.

Treatment with chaulmoogra oil, as in any other drug, must, of course, be continued for at least one year, and preferably longer, before any results can be ascertained. After reading a large number of articles on the chaulmoogra treatment, one becomes impressed with the claims of slow regression of lesions, shrinking of swollen, painful nerve trunks after local chaulmoogra ethyl ester injections, and reports of discharges of a fair percentage of patients. Yet, the statistics are so inconstant among different observers and in different regions of the world, and also the evaluation of results is made so difficult by the varying classifications of the types of the disease, that one hesitates to quote such statistics. Perhaps it is best merely to reiterate the statement of the 1938 Leprosy Congress: "Chaulmoogra oil from *Hydnocarpus spe-*

*ices* and its ethyl esters administered intramuscularly, subcutaneously and intradermally remains the most efficacious agent for the special treatment of leprosy.<sup>18</sup> (Of course, the newer drugs, sulfones and streptomycin, have appeared since then).

*Toxicity:* The toxic effects of chaulmoogra oil and its derivatives may be divided into several groups: (1) Immediate effects occur. These consist of coughing, choking and a sensation of dizziness. Although distressing, these symptoms are not important. (2) Next, there are local effects at the site of injection. They consist of inflammation of the tissues and even abscess formation. (3) There are also general symptoms, such as headache, malaise, and fever. (4) Respiratory tract symptoms, with chest pain and oppression and cough. These symptoms are the most important ones, for tuberculosis is the most common complicating disease of leprosy. Thus, pulmonary irritation must be avoided. Likewise, chaulmoogra treatment is contraindicated when a leprosy patient also has tuberculosis. (5) Another reaction which occurs following chaulmoogra reaction is the mysterious "lepra reaction",—a severe febrile attack preceding or accompanying new skin lesions. (6) Kidney disturbances have rarely been observed, but nephritis, another complication of leprosy, is a cause for caution in the pursuit of a course of chaulmoogra. Wade found the ethyl esters of chaulmoogra with 0.5 per cent of iodine added to give the least number of reactions of any of the varieties of chaulmoogra compounds.

*Histologic Changes:* After local intradermal injection of chaulmoogra preparations, mild inflammatory changes, with fibrinous exudate, monocytes, and a few polymorphonuclear cells were seen as well as yellow fat globules (chaulmoogra oil). These fat globules were present even several months after the injection.

*Other Fatty Acids (than Chaulmoogra Oil):* Other vegetable products besides chaulmoogra have received trials in the treatment of leprosy. Most of these crude or refined products are fatty acids or their



esters. Some of the chief ones tried will be mentioned briefly.

Gurjun oil, from the "gurjun tree", found in India, was given orally and applied locally to the skin lesions, but it proved of no value.

Beautherpy, in Venezuela, in 1871, had his own "treatment" consisting of the application to the skin lesions of Cashew nut oil (also, he used caustics, such as silver nitrate). The treatment was used even as far away as in Mauritius, but it soon fell into disrepute, for no beneficial results were produced.

Eucalyptus oil, in the form of external applications, likewise had no effect on leprosy.

In Central America and northern South America, the bark of the red mangrove of the genus *Rhizophora* was used orally in the form of an alcoholic extract, one teaspoonful twice daily. The dose was gradually increased to 8 or 12 teaspoonsful. Only temporary symptomatic relief occurred.

In Brazil, esters of the oil of the tree *Carpotrochea braziliensis* were given to lepers. In the Fiji Islands, ethyl esters extracted from the oil of the palm tree *Callophyllum bigator* were injected intramuscularly, once weekly, 5 to 8 c.c. per dose. Joint and nerve pains were relieved, and Neff, who used this oil, claimed that if the treatment was combined with chaulmoogra ethyl therapy, this combination of drugs was more effective than chaulmoogra alone.

Ichthyol, creosote, chrysarobin, resorcin, and pyrogallol have all been applied locally to leprous lesions. Inflammation of various degrees and even sloughing of the skin was produced. With milder degrees of inflammation, the local circulation was improved. This improved circulation apparently produced any beneficial effects therefrom (slow resorption of some of the lesions).

Rogers, in 1920, suggested that the action of chaulmoogra oil was due to its unsaturated fatty acid content. He, therefore, used other unsaturated fatty acids, and injected them intramuscularly. These oils can be divided into four groups: (1) Highly unsaturated fatty acids; cod liver oil, the

sodium salt of which was called sodium morrhuate by Rogers, was praised by him but later found to be too irritating for prolonged use. (2) Moderately unsaturated fatty acids; the ethyl esters of soya bean were shown to be very irritating and thus unsuitable for trial in leprosy. (3) Slightly unsaturated fatty acids; plain olive oil and ethyl esters of olive oil produced slight improvement in 25 per cent of patients in one series. (4) Almost saturated fatty acids; in this group coconut oil, plain and esterified, ethyl stearate, and ethyl margarate have been placed. They have no effect on leprosy.

During World War II, when it was impossible to obtain chaulmoogra oil from India, Degotte, in the Belgian Congo, substituted citronella oil. It was injected intramuscularly once a week, from 1 to 3 c.c. per dose, given for a period of 10 weeks followed by a therapeutic rest of two weeks. Degotte wrote that the results he obtained were as good as those he had noted with chaulmoogra oil.

*Arsenical Compounds:* When Ehrlich, in 1909, discovered salvarsan, the Wassermann test, published in 1906, was already known. Since many lepers give positive Wassermann (and Kahn) reactions, it was thought that salvarsan might also be effective against leprosy. The positive syphilitic serology is present in lepers free from syphilis and yaws and represents an unknown non-specific reaction. After trial of "606" in a number of small series of leprosy patients, Ehlers,<sup>19</sup> Gioseff,<sup>20</sup> de Vertenil,<sup>21</sup> Wellman,<sup>22, 23</sup> Sandes<sup>24</sup> and Montesano,<sup>25</sup> all expressed complete disappointment in this drug as related to the treatment of leprosy. Since 1912 it has not been used.

*Mercurial Compounds:* Around the turn of the century, when syphilis and leprosy were confused, so-called "syphilitics" who later turned out to be lepers were sometimes treated with mercuric perchloride, one intramuscular injection of 1/5 gr. per week. Two nerve-type lepers treated by Crocker showed only slight improvement. (For a discussion of the organic mercurial compounds, see under "Aniline Dyes"). Mer-

curial compounds have been dropped from the list of antileprotic drugs.

*Antimony*: In 1921 Cawston gave intravenous tartar emetic (2 per cent solution) in doses of 2 to 5 c.c. bi-or tri-weekly. He reported several instances in which leprosy ulcers healed and anesthetic skin areas became hypesthetic. He also used colloidal antimony (oscostibium), giving it intravenously in bi-weekly doses up to 12 c.c. Wildish<sup>26</sup> reported on these drugs after two months' use and noted "encouraging decrease in size of ulcers" and lessening of anesthesia. Hoffmann suggested stibosen as an adjunct to chaulmoogrates. Rodriguez gave 1 per cent tartar emetic to 31 patients intravenously for six months, observed no improvement. His dosage ranged from 0.5 to 2.5 c.c. per week. Paldrock also, after a small clinical trial found fuadin without any effect.

At the National Leprosarium, 5 gm. intravenous fuadin are given to alleviate acute lepra fever, and the drug is found to be of value; often it ends the reaction within one day (personal communication).

*Copper Salts*: Cyanocuprol, after its beneficial effect was demonstrated in experimental animal tuberculosis, was tried on lepers in Japan by Kroga, also by Takano. They noted some softening and shrinking of nodules. Trocello showed that the drug produced fibrosis and lymphocytosis in experimental tuberculosis. Dho, in Italy, tried cyanocuprol, 2 per cent solution, given intravenously daily, on 20 patients. In the lesions he found proliferation of fibrous tissue and granulation of lepra bacilli. Many nodules became smaller in one to two months, but none of the patients became "arrested".

*Gold Salts with Carbon Dioxide Snow*: Gold salts were first used in leprosy by Dehio in Esthonia in 1914. In 1926, Paldrock, also in Esthonia, theorized that if leprosy bacilli were frozen, antigens should be set free and antibodies would be formed by the body and leukocytes mobilized in response to these antigens, and immunization thus obtained. He applied the carbon dioxide locally to the skin and reported five pa-

tients discharged as "well" after two years of such treatment.

The carbon dioxide snow is applied monthly for three to four seconds to each of ten lesions. After four monthly treatments the patient gets a therapeutic rest for four months. The carbon dioxide, Paldrock further postulated, stripped the bacilli of their capsule, and then these "denuded" bacilli could be attacked by heavy metals. Sanocrysin, a gold salt, proved to be a failure. Solganol, given concomitantly with carbon dioxide snow, produced lymphocytosis. Krysolgan, given by Eubanas to ten patients, showed "unequivocal results" after six months. It was administered as 0.0001 gm. intravenously, repeated at 10 day intervals. Triphal, another gold salt, gave no improvement.

Hoffman pointed out the value of gold salts in lepromatous ocular lesions to promote resorption. Kupffer observed small rises in temperature shortly after gold salt injections. He gave an initial dose of 0.001, later increased to 0.01, then 0.02 gm. every eight days. After three years, corneal, iris and fundal lepromata had disappeared.

Solganol has been administered in doses of 0.1 to 0.5 c.c. intramuscularly once to twice per week. The patients so treated were much too few in number to make any conclusions of value. Gminder was not successful with solganol. Pooman and Amies, however, reported marked improvement in about half of their patients. Lopion, a similar gold salt, was administered weekly by intravenous injection.

Golorine, writing in 1940, reported that he found toxic reactions so numerous with the use of the gold salts (skin eruptions, agranulocytosis and aplastic anemia) that he stopped using them. He found "auro-detoxin" not toxic and reported the beginning of a series of treatments with this compound. It was administered bi-weekly intramuscularly, with 0.05 gm. increased to 0.5 gm. weekly until 5.0 gm. were given.

Paldrock, in an article in 1933, modified and extended his former theory on the action of carbon dioxide snow and gold salts on leprosy. He reasoned that the differ-



ences between tubercle and leprosy bacilli consisted in: (1) a greater amount of free nucleic acid and karyoproteids in leprosy bacilli; (2) more firmly combined plasteoproteids in leprosy than tubercle bacilli, and (3) the presence of lipoproteid with Gram-positive and Gram-negative lipoid lacking in tubercle bacilli. Paldrock therefore postulated that the leprosy bacilli actually contained nuclei, similar to fungi, and had a surrounding membrane. In fact, he considered the organism to be a fungus. Therefore, if this membrane could be removed, the nucleus would become accessible to antibodies. The colloids of the membrane should be broken down by freezing (with carbon dioxide snow). Polymorphonuclear proteases and lymph lipases then destroyed the remaining membrane colloids and the "nuclei" of the bacilli. Leukocytosis was marked. "Carbon dioxide snow treatment of leprosy is an active autoimmunization and therefore a specific remedy in leprosy."<sup>27</sup> If there was a standstill of improvement after two years' of snow treatment, Paldrock then used the gold salts as a new irritant. These salts, he believed, split the Gram-positive lipoid acid.

Only Paldrock and his associates have attained any success with this treatment. Its efficacy is not subscribed to by any other investigators.

*Nastin*: In 1904, Deycke and Reschad Bey cultured some acid-fast bacilli from human leprosy tubercles, ether-extracted the organism. The fatty portion, when injected in several lepers, had a beneficial effect. This substance was found to be a fatty acid glyceryl ester, melting at 48° to 50° C. Deycke called it "nastin." When injected in patients, nastin gave a pronounced leukocytosis in those who reacted, leukopenia in those patients who did not react. There was also local inflammation and fever. When injected with cinnamon acid nastin produced no leukocytosis. The authors therefore concluded that the leukocytosis was not necessary but that the organism used the leukocytes to gain the active agent from the above acid (found in balsam of Peru). In the body, the acid is oxidized by benzoic

acid, but the latter is inactive. Therefore an intermediate compound, benzaldehyde, was used. Deycke and Reschad Bey concluded that the benzoyl radical was the substance which activated nastin. Benzoyl chloride easily splits off the benzoyl radical. Therefore, it was dissolved in olive oil with nastin. Without nastin, benzoyl chloride is of no value, since it will probably combine with other fats long before it reaches the lepra bacilli. Nastin will be more effective if combined with benzoyl chloride, for then it will not have to depend on the leukocytes to obtain the benzoyl radical. Once thus defatted, the bacilli are easily destroyed by the body.

The ration of nastin and benzoyl chloride is important, according to Deycke. If an excess of nastin is present, the patient has severe fever reactions and local inflammations with suppuration. Such reactions are not found if there is an excess of benzoyl chloride. Rather, leprous nodules slowly recede, and several patients with nerve type lesions had some regression of skin anesthesia.

The proper ratio is nastin, one part and benzoyl chloride, 30 parts or more. Deycke was convinced that with this treatment the patients became immunized. The combination of nastin and benzoyl chloride was called nastin B. For administration, a dry syringe is necessary (or, if the syringe is wet, the benzoyl chloride will form hydrochloric acid, and necrosis at the injection site occurs). Treatment is begun with nastin B<sub>1</sub> (an excess of benzoyl chloride), 4 c.c. containing 0.5 mg. once a week, later given more frequently. Nastin B<sub>2</sub> (excess of nastin) is used in small lesions resistant to nastin B<sub>1</sub>. Reactions occur. It should therefore not be used in nerve leprosy or in leprotic eye involvement.

In small groups of patients with nodular leprosy, Kupffer, Ziemann, T. S. B. Williams, Rudolph, and Scott had good results (marked regression of nodules) in five to ten months of treatment. McLeod, Thompson, Brinckerhoff, and Kiwull in similar small series of patients got only febrile re

actions and local inflammations but no distinct improvement of their patients.

In 1909, Deycke went to the Government Leper Colony in British Guiana to initiate his nastin treatment in 503 patients there. He reported improvement in two-thirds of the nerve type, two-thirds of the nodular type, and two-thirds of the mixed type of leprosy patients treated. After four months, Deycke left Guiana to return to Germany. In a follow-up report three and one-half years later, the local Guiana leprologists, Wise and Minett, reported that of 250 patients still being treated by nastin, only four "cures", were recorded and one of these patients had meanwhile died and another had a recurrence of the disease. Wise and Minett reported that in the first three to six months of treatment mental improvement, better appearance of the facies, softening of the nodular lesions, slight decrease in the size of the infiltrations, and a slight increase in sense of touch in anesthetic skin areas occurred. However, improvement then stopped, and regression occurred in the next few months to the original pre-treatment state.

*Tuberculin*: Koch, in 1890, electrified the medical world with his discovery of tuberculin, a filtrate from glycerol-broth cultures of human tubercle bacilli. He advocated it as a possible immunizing agent against tuberculosis and tried it in the treatment of tuberculosis (with no success, as later became apparent). *M. leprae* being similar to *M. tuberculosis* in structure, several leprologists decided to try tuberculin in the treatment of leprosy. Goldschmidt found that seven of his twelve patients got severe febrile and local reactions from injection of 1.0 mg. of tuberculin, and the other five showed no improvement. V. Babes, treating five patients, also noted severe febrile reactions. His patients showed slight temporary improvement after the febrile reaction. Truhart's report was similar to the other two. Use of tuberculin in the treatment of leprosy was abandoned.

Rou, in 1926, gave weekly injections of 0.25 mg. autolysed tubercle bacilli, noted a mild febrile reaction. In five patients, two

had resorption of nodules in one and one-half years of treatment.

Davidson injected tubercle endotoxoid in ten lepers, observed no improvement in nodular type patients but improvement of anesthesia in those with the nerve type of leprosy.

*Bacterial Vaccines*: In 1896, Carasquilla inoculated a goat with leper serum, later bled the goat, and injected the goat serum in fifteen patients, beginning with 0.5 c.c. and increasing the dose to 20 c.c. after one month. Eight to twelve injections, extending over six weeks, "cured" all of these patients, (nodules and anesthetic spots disappeared). No other investigator has ever been able to repeat Carasquilla's work.

Rost cultured an acid-fast bacillus from leprosy lesions, injected it in a monkey and recultured an acid-fast bacillus from skin nodules on the monkey. This culture material he injected into ten patients with maculo-anesthetic leprosy, six of whom were "improved." Injections were given weekly in amounts of 5 c.c. of the sterilized culture material. After one year of treatment, five of twenty-two patients had recovered, fifteen were improved; two-thirds of these patients had the maculo-anesthetic type, the others the nodular type of leprosy.

Temporary improvement (softening of the nodules) in nodular leprosy was reported by Kraus in 1923 following local inflammation subsequent to the injection of acid-fast bacilli grown in culture by Duval and Deycke. Of nineteen patients, two showed this beneficial action. Walker, Haddon, A. W. Williams and Gohar, reported series of a few patients treated with similar vaccines and recorded only temporary decrease in size of nodules with softening but no permanent cures. Reenstierna, in 1936, treated a total of ninety patients in Venezuela and Colombia with a vaccine prepared by him from an acid-fast bacillus culture. Unfortunately, he observed the results for only three months. In two to four weeks the nodules softened, decreased in size. Eighty-seven per cent of patients with anesthetic skin areas had a partial return



of sensation. The course of treatment consisted of three injections of 10 c.c. each in one week.

In 1921, Roussel, of New Orleans, upon the suggestion of Campos, used anthrax vaccine in the treatment of two patients. It was given subcutaneously, beginning with a 0.25 c.c. bi-weekly dose increased to 1.5 c.c. in five weeks. The local lesions became inflamed, later disappeared completely within two months. In 1935, these two patients, who had the maculo-anesthetic type of leprosy, were still living and healthy.

**Protein Shock Therapy:** It may be argued that nastin, anthrax vaccine, and other bacterial vaccines should have been discussed under this title. However, since the users of these drugs have not claimed their action to be due to the febrile reaction which often attended their application, I have classified them separately. The substances mentioned below, however, act by producing febrile reactions.

Snake venom has had small trials in the treatment of leprosy. According to ancient Hindu mythology, a leper bitten by a snake is cured. In 1892, Carreau reported the case of a leper bitten by a venomous snake whose tuberculoid lesions disappeared. Dyer, of New Orleans, treated five patients with cobra antivenene. He began with 1 c.c. injected subcutaneously every other day, increased the dose to 10 c.c. every day. The lesions markedly diminished in size in all the patients in one to two months' time. Woodson and de Moura reported similar beneficial results. Goldschmidt emphasized that it was the febrile reaction produced by the administration of the venom which was probably responsible for the effect on the disease. Lewin went a step further and expressed the opinion that the injection of any foreign protein would produce a like result. Couhan, in 1938, found cobra venom effective in alleviating peripheral neuritis of leprosy in 60 to 80 per cent of his patients.

Erysipelas toxin, given in slowly increasing doses, proved of no value.

Typhoid-paratyphoid A-B injections also produced severe fever with temporary remission of leprosy afterward.

Injections of sterile milk, starting with a dose of 0.5 gm. increased up to 10 c.c. intramuscularly twice weekly were given by Drew to 36 patients, of whom he was able to discharge seventeen. Dyce-Sharpe also used it. Sarkar wrote that milk injections gave relief from neuralgia and joint pains of leprosy. Gomes likewise observed a diminishing in size of nodules and tuberculoid lesions in a series of 33 patients after one month of milk injections.

**Iodine:** Iodides (sodium and potassium) were first used by Danielssen and Boeck in Norway in 1848. They discovered that severe febrile reactions occurred in the patients thus treated. Diesing and Courtney (1900) used iodoform in olive oil, reported no reactions. In 1908, Marchoux and Bourret observed that lepra bacilli were discharged from the nose during such a reaction. They looked granular and had lost some of their acid-fastness. Several investigators, especially Rogers and Muir, noted a clinical improvement after such a reaction. Muir, in 1923, began his work on the iodide treatment of leprosy. He controlled the febrile reactions produced by the iodides by administration of tartar emetic (intravenously) and the painful symptoms of subcutaneous adrenalin injections.

Iodide reactions are considered harmful by many leprologists. Muir, however, considers them beneficial if the dosage is well-regulated. Iodides cannot be used in mass treatment; their dosage must be individualized. Muir begins with a small dose and slowly increases it to tolerance. Iodides are especially good to break down large amounts of lepromatous tissue, and immunity is thus increased. Signs of a reaction are:

- (1). Swelling and erythema of the lesions.
- (2). Appearance of fresh nodules, often painful.
- (3). Fever.

(4). Markedly increased sedimentation rate.

(5). Granulation of bacilli.

Potassium antimony tartrate (0.02 gm. intravenously every other day) controls the reaction; 0.3 c.c. adrenalin in 3 c.c. saline (intramuscular or intravenous) stops the nerve pains. Muir suggested the following potassium iodide dosage:

(1). Begin with 1 gr. per day and increase it by 1 gr. until the temperature rises above 99.0° F., or there is swelling and redness of the lesions.

(2). When the swelling and fever go down, continue on the same dosage but give only once or twice a week.

(3). When 20 gr. are reached, increase the dosage by 5 gr.

(4). When 60 gr. are reached increase the dosage by 30 gr.

Iodides were used by Muir in the diagnosis as well as treatment of leprosy. Lepers showed a febrile reaction when given iodide. "The action of the iodides in some way removes the protective mechanism which shuts off the bacilli from the tissues."<sup>28</sup> Only lepromatous patients in good general health who will be able to withstand the strain of the febrile reaction should be treated with iodides.

Canaan explained the iodide reaction to be due to killing of many bacilli, whose toxins then entered the blood stream; nodules break down, and a bacillema is produced. Canaan abandoned the iodide therapy and agreed with Cochrane, who wrote: "When iodides were introduced it was hoped that they would hasten the resolution of the disease, but in my experience patients treated with potassium iodide showed no more rapid subsidence of their leprotic infection"<sup>29</sup> (than those treated with chaulmoogrates).

*Aniline Dyes:* Aniline dyes have been used as antiseptics since the turn of the century. In 1929, Hoffman used rivanol, an acridine dye, as a powder in open leprosy lesions. Several such lesions healed up over a period of three months. Hoffman therefore thought that it had some beneficial action but ascribed this action to destruc-

tion of secondary invaders rather than lepra bacilli.

Denny and Muir found the intravenous administration of mercurochrome effective in treating lepra reactions. Ryrie, working in Malaya, thereupon speculated that the abortion of lepra reaction with mercurochrome was due to its fluorescein content, and the fluorescein was taken up by the macrophages in the leprotic lesions and interfered with the process deriving from the attachment of antibody to the cells. He preferred to give fluorescein to mercurochrome, because the former could be given safely in much larger doses. He gave 10 c.c. of 2 per cent aqueous solution intravenously twice a week. The lepra reaction stopped in 24 to 48 hours in 42 per cent of the patients. The others had remission in two to three weeks, and in this time, according to Ryrie, the reaction would probably have ended spontaneously. In a subsequent series of patients, Ryrie injected intravenously phthalic acid, the active ingredient of fluorescein. In 62 per cent of the patients, the lesions decreased in size in two months. Ryrie therefore suggested a course of six weeks fluorescein between courses of chaulmoograte esters.

Ryles noted the sensitizing action of aniline dyes to the skin to enhance the effects of ultraviolet rays. He hoped this combination of ultraviolet ray enhancement and antiseptic properties would show the dye, brilliant green, useful in leprosy therapy. He sprayed the dye (1:10,000) on leprosy ulcers. The ulcers readily healed. Then he gave the dye intradermally, and two-thirds of his 455 patients so treated improved. The dosage used was 5 to 8 c.c. of 1:2,500 solution with 1 per cent novocaine given once weekly, then given two weeks' rest. Ryles found "Bonney's blue" even more effective than brilliant green. Bonney's blue consists of:

Brilliant green powder	0.5 gm.
Crystal violet	0.5 gm.
Absolute alcohol	25.0 c.c.
Distilled water to	2500 c.c.

The crystal violet is added to the alcohol, then added to the rest.



Legate also noted considerable regression of lesions in ten patients with nerve type leprosy after several months' treatment with Bonney blue.

Rao and Roy found Bonney's blue, brilliant green, trypan blue, and fluorescein ineffective in their patients.

Emerson et al., in 1934, investigated the activity of the aniline dyes *in vitro* on various acid-fast bacilli and found them all (merthiolate, mercurochrome, metaphen, methylene blue, octyl resorcinol) quite active except trypan blue. They also showed that severe nephritis was produced by these dyes in experimental animals and therefore cautioned their use in lepers, since nephritis is one of the complications of leprosy. Nausea and vomiting also occurred in clinical cases.

Montel, in 1934, treated a few patients with intravenous methylene blue. His "successes" were later withdrawn when a second larger trial gave no beneficial results. In 1940, Dharmendra found that methylene blue carried no effect on rat leprosy nor *in vitro* cultures of acid-fast bacilli.

Since then, no reports of any further work with these dyes have been published, for they have not proved themselves of value.

#### VITAMINS

Thiamin chloride (vitamin B<sub>1</sub>) has been reported on in the treatment of nerve leprosy by several authors. Muir and Henderson noted that rat leprosy was often accompanied by hypovitaminosis and that B<sub>1</sub> had a pathogenic and therapeutic relationship to nerve leprosy, and they showed that rat leprosy could be more readily induced in animals in the presence of hypovitaminosis. Vitamins A and C had no effect, but the B group had a definite relationship to this phenomenon. Badger and Sebrell showed that vitamin B<sub>1</sub> was responsible.

Brown, in Nigeria, treated 66 lepers with addition of yeast to their diet, later injected vitamin B<sub>1</sub> intramuscularly and noted "improvement in 43 per cent" of these patients. He pointed out the poverty of B vitamins in tropical diets. Bacu noted improvement of nerve pain and lessening of skin anesthe-

sia after four weeks of yeast administration. Bacu emphasized the clinical similarity of nerve leprosy and beriberi (peripheral neuritis, muscle paralysis, trophic disturbances). Another interesting speculation of his concerns the higher intake of carbohydrate in the tropics with therefore greater vitamin B<sub>1</sub> demand for metabolism of these carbohydrates. Beriberi is most common in the tropics. Also in the tropics the nerve type of leprosy is much more frequent than the nodular variety, which latter is seen in the majority of lepers living in the temperate zones. Bacu gave 5 to 10 mg. thiamine chloride (subcutaneous or intramuscular) daily, observed improvement of neuralgia in nerve lepers after two to three weeks. A diet with yeast, unpolished rice, wheat germ, green vegetables to furnish vitamin B<sub>1</sub> was introduced.

Villela, Badger, Gminder, Bleuth, and How, also were able to alleviate acute peripheral neuritis in leprosy with thiamine injections, but they all agreed that none of the other symptoms of leprosy were relieved. How suggested that vitamin B<sub>1</sub> deficiency may predispose to nerve injury by the lepra bacilli.

#### DIPHTHERIA ANTITOXIN AND TOXOID

In the middle 1930's Oberdoerffer, a German leprologist, read of some work done by A. Clark, who had drawn attention to certain toxic properties of colocasia (or cocoyam or taro root, a food plant of the genus *Xanthosoma*, usually species *sagittifolium*). Clark ascribed the general debility of taro-fed people to these toxic properties, residing in an acid sapotoxin. Acute poisoning with colocasia, he found, produced "glomerulo-tubular nephritis and marked degeneration of the adrenals". The sapotoxin, he discovered, hemolyzed blood *in vitro*. He also demonstrated that the highest degree of toxicity of the plant occurred at the end of the dry season. Instantaneously killed animals showed marked adrenal degeneration. This adrenal destruction Clark considered the immediate cause of death.

Oberdoerffer, working in Nigeria, noted that nerve leprosy most often cropped out

at the end of the dry season, the time when the native people ate the most colocasia. He then proposed the theory that adrenal damage, as for example caused by colocasia consumption, predisposed to leprosy. With this idea in mind, he searched for an "adrenal-protecting" substance. Since diphtheria toxin destroys the adrenal, the antitoxin, he argued, must have a protective power. Therefore, when he went to the Siam Leper Colony in 1938, he, Collier and McKean treated a group of patients with 6,000 units of diphtheria antitoxin for forty daily doses. Later, 2,000 unit injections were given every tenth day. They noted decrease in and flattening of the nodules, often scaling over, and gradual shrinking. Tetanus antitoxin had no such effect.

Next, Oberdoerffer and his associates tried a group of patients on diphtheria toxoid and again observed the shrinking of the nodules after two to four weeks of treatment. The nerve leprosy patients had a reduction in size of their enlarged nerve trunks and partial return of sensation of anesthetic skin areas. Fragmentation of bacilli in the lesions occurred. The dosage of the toxoid was 1 c.c. every two weeks, increased by 0.5 c.c. until a maximum of 3 c.c. was reached. Fifty per cent of the patients became symptom-free (78 patients) in ten months and were discharged. McKean reported that better results were obtained in the nerve type than in the nodular type of leprosy.

Other investigators—Schujman and Mercieu, Moiser, Davison and Grasset, found the diphtheria toxoid ineffective. Carpenter et al. found it had no effect on rat leprosy. Muir suggested that Oberdoerffer, Collier, and McKean got such spectacular results because they mistook early tuberculoid for lepromatous lesions and were therefore merely observing numerous spontaneous recoveries from leprosy, often seen in early tuberculoid nerve type.

In a personal conversation with Dr. McCoy, he recalled a meeting he had with Dr. Collier in which the latter showed him photographs of the "before" and "after" appearance of these Siamese lepers treated

with diphtheria toxoid. Dr. McCoy could see no difference in the pre- and post-therapeutic pictures and thought that Dr. Collier had been so influenced by his own enthusiasm for the treatment that perhaps, in being partial to it, he had almost "imagined" improvement where an impartial observer could see none. Dr. McCoy then devised a controlled experiment, with one-half of the patients receiving *placebo* injections, judged by himself for results (he assuming the role of an impartial observer) to be run for one year at the Carville Leprosarium. The results were summed up by Faget and Johansen: "From close observation of 35 patients treated with diphtheria toxoid for one year under carefully controlled conditions and from the observations of 195 other patients treated with diphtheria toxoid from six to fifteen months, it is concluded that this treatment has no beneficial therapeutic action in leprosy and is even fraught with danger to the patient."<sup>30</sup>

#### SULFONE DRUGS

In the early days of sulfonamide drugs, prontosil and soluseptacine, the latter given in intramuscular injections of 5 to 10 c.c. each, were shown to clear up secondary infections but to have no effect on the lepra bacilli themselves.

Sulfanilamide, given in doses of 2 gm. per day for six weeks at the Carville Leprosarium, was abandoned. Its administration was accompanied by anemia, drug fever in over one-half of the patients, lepra-reactions, and conjunctivitis. There was no apparent effect on the leprosy itself, but secondary infections healed. In rat leprosy sulfanilamide had some beneficial effect, for Krakower found that he could inhibit the disease in all his animals with this drug, but the disease reappeared as soon as the animals were taken off sulfanilamide. Krakower's conclusion therefore was that sulfanilamide is bacteriostatic rather than bacteriacidal in action on *M. leprae*.

Promin, a sulfone drug, was first used in leprosy in 1941. It is called Na salt of p,p'-diaminodiphenyl-sulfone-N,N'-di-(dextrose sulfonate).



W. M. Simpson was the first to suggest that it be tried to influence the regression of rat leprosy nodules. After this work was started, Feldman, Hinshaw and their associates at the Mayo Clinic reported that tuberculous guinea pigs treated with it lived longer and showed less extensive lesions than the controls. Condry noted similar hopeful signs in a series of rates inoculated with rat leprosy.

Hinshaw and Feldman treated 36 pulmonary tuberculosis patients with oral promin over one year's time. Eight patients (20 per cent improved markedly, 14 (33 per cent) slightly, eight (20 per cent) remained stationary, and eight (20 per cent) became worse. The series was too small to evaluate promin in the treatment of tuberculosis, but Hinshaw considered this result somewhat encouraging.

At the Carville Leprosarium, promin treatment was begun under the direction of Faget in 1941. Because the oral administration of the drug (1/2 to 1.0 gm. per day) soon produced severe hemolysis and anemia, intravenous injection was tried. One to 5 gm. per day for six days per week were given. Most patients tolerated the 5 gm. dose. One week out of three the patients "rested" (no promin was given). Promin blood levels decreased rapidly, so that only traces of the drug remained after six to eight hours. Toxic manifestations appeared after about six weeks of treatment. The most important ones were a slow erythrocyte destruction. A blood count must therefore be done twice a month. In 71 per cent of the patients erythrocyte count fell below the 3,500,000 mark, below 3,000,000 in 9 per cent. Antianemic treatment was successful in most cases, and the promin did not have to be stopped. Oral iron and liver extract were effective in controlling the anemias, but occasionally an anemia was so severe that it was necessary to give oral iron and parenteral liver extract. When the erythrocyte count dropped below 3,000,000 promin was stopped temporarily while the iron and liver extract were given and later cautiously resumed in reduced (1 to 2 gm.) doses.

Leukopenia occurred in 3 per cent of the patients. There were no urinary disturbances, but because nephritis can be caused by sulfonamides, urine examinations were done every two weeks. Other toxic reactions included maculo-papular dermatitis in 16 per cent of the patients. Desensitization (beginning with 0.1 gm. and increasing the dose to 2.0 gm. over a two month period) was successful. Allergic rhinitis, headaches were less common complaints. Nausea occurred in 35 per cent, could be prevented by injecting the drug slowly. Acute lepra reactions were less frequent than they had been with any other previous form of treatment. A few patients had exacerbations of iridocyclitis followed by improvement.

Of 68 patients, most of whom had moderate or advanced lepromatous, mixed or nerve leprosy, 41 (60 per cent) were improved, 23 (32 per cent) stationary, and four (8 per cent) worse. "Control" patients were definitely in poorer health. "Promin is an advance in the right direction", Faget et al. wrote.<sup>31</sup>

In a follow-up report in 1945, Faget and Pogge noted "continued improvement" of the patients observed earlier. There were now 137 patients under promin therapy, of whom 80 (58 per cent) were improved. Those under treatment less than six months only showed 26 per cent improvement. Those under treatment showed an improvement rate of 71 per cent. Sixty-two patients on promin more than one year had a reversal of bacterial skin smears from positive to negative. Certainly, the authors concluded, the drug is more beneficial than anything else tried so far. Whether its action is chemotherapeutic remains to be seen. Faget (personal communication) believes 25 per cent of patients will improve in the first year of promin therapy, 50 per cent in the second, 75 per cent in the third, and 100 per cent in the fourth.

Fite and Gmear studied the skin biopsies of patients treated with promin at the Carville Leprosarium. They reported: "The important finding is that promin appears to eliminate bacillary infections of the blood vessels and blood stream, thereby pre-

venting the formation of new lesions. Those lesions with the richest blood supply show most atrophy. A more powerful bacterial agent than promin appears to be necessary for the chemical destruction of bacilli within tissue cells, and especially those within globi."<sup>32</sup>

Wharton, who observed great improvement in seven advanced type lepromatous patients, found that the lepromatous tissue after treatment became fibrous connective tissue. Wharton theorized that the destruction of lepromatous cells makes it impossible for the bacilli to multiply.

Smith, McCloskey and their associates, ran an interesting chemotherapeutic experiment with combined streptomycin and promin in guinea pigs infected with human tuberculosis. They calculated the therapeutic index of streptomycin against tuberculosis to be ten times as great as that of promin. By combining the two drugs, they obtained an effect three times as great as they had expected. Therefore they wrote: "The results of treatment with the combination of streptomycin and promin appear to indicate a synergistic action rather than simple summation of effects."<sup>33</sup> This observation may prove to be of interest in future investigations on the effect of these drugs in leprosy.

Another sulfone drug now being used in the treatment of leprosy is diasone. This is the disodium formaldehyde sulfoxylate derivative of diaminodiphenyl sulfone. It was first synthesized in 1937. Callomon, in 1943, reported that it inhibited the progress of experimental tuberculosis in guinea pigs and was less toxic than promin. Feldman's observations were similar. Petter and Prenzlau found it useful in clinical human tuberculosis. They treated 108 patients with 1 gm. per day, given orally. The blood levels averaged 2 mg. per cent. Toxic reactions consisted of headache, malaise, gastric upset, and mild anemia. Almost all the patients "improved", even those with far-advanced tuberculosis. Olson, in 10 tuberculous patients treated for one year, noted no improvement.

At the Carville Leprosarium, Faget et al. began the use of diasone in 1944. They began the treatment with 1/3 gm. given orally three times a day but found that several patients developed a hematuria. Then the beginning dose was reduced to 1/2 gm. per day and increased to 2/3 gm. in two weeks and 1 gm. in three to four weeks. Over a two and one-half year period 104 patients were treated, of whom 66 have been on diasone six months or longer. Seventy-four per cent had the lepromatous type, 20 per cent mixed, and 6 per cent neural leprosy. In 81 per cent the disease was moderate to advanced; 24 per cent of the patients became bacteriologically negative; improvement was present in 65 per cent; questionable improvement in 12 per cent, and no change in 23 per cent. None of the patients became worse. Treatment had to be discontinued in 30 per cent because initial hematuria, eczema or vomiting occurred. Diasone is about as effective as promin in leprosy, according to Faget, and has the advantage of being an orally administered preparation. Muir observed an increased tolerance with continued diasone administration accompanied by a decreased bleed level. Perhaps, he suggests, that is why anemias occur only rarely after the initial administration. Smith, in 1943, found a lowering of threshold of renal secretion of diasone in experimental animals. This may be a factor in lowering blood levels. If this is the mechanism involved in lowering the blood levels, it is necessary to find out what period of non-administration is necessary to restore the original blood level.

Promizole, another sulfone drug, 2,4'-diamino-5 thiasolphenyl sulfone was also tried in experimental tuberculosis. The results were the same as with promin. However, there were no toxic reactions, but the animals' thyroid gland became diffusely enlarged. Hinshaw gave 10 to 16 gm. per day orally to tuberculous patients without toxic manifestations.

Promizole was introduced at the Carville Leprosarium in 1945 because it had given encouraging results in skin tubercu-



losis and also had been relatively non-toxic. Seven patients were treated for one year; eight for six months. The beginning dose was 0.5 gm. three times a day per month, slowly increased to 2 gm. three times per day. Improvement occurred in all the patients, but the skin smears were still positive for bacilli. Further trial is needed to evaluate the drug.

#### ANTIBIOTICS

Penicillin was tried on seven patients at the Carville Leprosarium in daily doses of 50,000 to 100,000 units for one month. When no beneficial effects resulted, the dosage was increased and the drug continued another month. Still, there was no effect. It was therefore concluded that penicillin had no influence on leprosy. In trials in Spain and Latin America similar conclusions were reached. It is, however, effective in controlling secondary infections.

Waksman and his associates found streptomycin, an extract from meat-broth (or corn-steep liquor) cultures of *Actinomyces griseus*, to inhibit growth of *in vitro* cultures of human and avian tubercle bacilli, in addition to other organisms. Since their report in 1944, several trials of the drug on experimental tuberculosis in guinea pigs have shown that the treated guinea pigs showed only minimal tuberculous lesions while control animals had multiple large lesions and usually died. Even after the disease had been allowed to progress for six weeks in one series, treatment begun at that time saved 23 out of 25 animals, while 17 of 24 controls died. In clinical tuberculosis, streptomycin has so far proved to be a "hopeful" drug, but experience with it is still too short to make evaluation possible. Feldman and Hinshaw treated 34 patients with 100,000 to 150,000 S-units intramuscularly every three hours. Those patients with fine, disseminated pulmonary tuberculosis showed much roentgenographic improvement after six to eight weeks. Urinary tract lesions cleared up in three out of four instances. Old, fibrotic lesions and cavities were not affected. There were several relapses after cessation of therapy. The au-

thors, therefore, considered the drug bacteriostatic rather than bacteriacidal.

Since tuberculosis and leprosy are caused by similar organisms and have a number of pathogenic characteristics in common, it was only natural that streptomycin should also be tried in leprosy. Ten patients at the Carville Leprosarium were placed on 1 gm. intramuscular streptomycin six months ago. So far, no results have been published. Two months ago, on the writer's visit to Carville, he was told that there had been slight shrinking of some lesions of these patients, but no conclusions could at that time be drawn. The treatment, of course, is very expensive—about \$1000.00 per patient per month. Only time will tell what the results will be. Most of the patients had the feeling of dizziness described under the toxicity effects of streptomycin and one also had transient nerve deafness. Several of these patients are being treated with both promin and streptomycin.

For the treatment of the trophic ulcers of leprosy a new method has been devised at Carville: streptomycin broth culture filtrate is applied as a wet dressing to these ulcers, and they have healed in a few weeks, whereas leprotic ulcers have always been more or less refractory to any treatment. Whether the streptomycin kills secondary invaders or inhibits the lepra bacilli themselves is not known.

Johnson and Burdon recently reported a new antibiotic, Eumycin, extracted from certain strains of *Bacillus subtilis*. It inhibits *M. tuberculosis* cultures (both human and avian) in high dilutions. It is now being investigated by Fite in experimental rat leprosy.

#### SUMMARY

There are some three million lepers in the world, most of whom are in India and China. The disease is only mildly contagious and is usually contracted after a long period of close contact with a leprous patient. Eighty per cent of lepers come from a home in which a leprous family member lives. The incubation is less than five years in four-fifths of the cases. The disease is caused by the acid-fast bacillus, *Mycobac-*

*terium leprae*. The principle clinical types are nodular (lepromatous) and nervous leprosy. The nodular type is more severe than the nervous, but both carry an unfavorable prognosis. Tuberculosis and glomerulonephritis are the two chief complications of leprosy.

Prophylaxis of leprosy has traditionally been conducted chiefly through segregation of leprosy patients, and voluntary segregation has been most successful. The "general" treatment is the most important aspect of the therapy of leprosy. A diet especially rich in proteins and vitamins and well-supplied with carbohydrates and fats is important. Work and recreation must be offered in leprosy institutions.

Specific drugs are difficult to evaluate because the disease has such a prolonged course and sometimes remissions. Also, some patients exhibit more resistance than others and therefore may even spontaneously recover.

Chaulmoogra oil is the drug that has been most widely used in the treatment of leprosy. The oil is derived from trees of the family *Flacourtiaceae*, in particular from the seeds of *Hydnocarpus* and *Taraktogenus* species. The oil formerly was used orally. Ethyl esters of the various fatty acids contained have been used most widely. They are given intramuscularly, subcutaneously, or intradermally. The sodium salts of these fatty acids have also been injected, especially intravenously. The mode of action, according to some authors, is due to the pentacycle carbon ring. Rogers, on the other hand, thought the effects were due to unsaturation of the fatty acids. Oral dosage produces nausea and vomiting, and local inflammation occasionally follows injection. The effect of the oil on the disease is almost impossible to evaluate from present reports. The International Leprosy Congress in 1938 considered chaulmoogra oil, and especially its ethyl esters "the most efficacious drug" then known. No specific effect was claimed.

Other vegetable and animal fatty acids have been largely discarded. Those used included sodium morrhuate, oil of eucalyptus and oil of citronella.

Various metal salts have been tried. The frequently positive Wassermann test suggested some relationship to syphilis, later proved to be false. Arsenicals were shown to be of no value, as was found to be true also of mercurials. The only antimony compounds still used are tartar emetic and fuadin, used to treat acute lepra fever. Copper salts have only been rarely tried. Paldock froze the local lesions with carbon dioxide snow and then gave organic gold salts. He recommended the gold salts particularly in the treatment of leprosy eye lesions. He claimed to have obtained numerous arrests of the disease.

Vaccines against leprosy have failed to affect the disease except in so far as they produced protein reactions. Nastin, tuberculin and various other bacterial vaccines are such substances.

Protein shock has been produced by snake venom, milk, erysipelas toxins and typhoid vaccines. All these give a more or less severe reaction. Any benefit obtained is derived from such reactions.

Iodine similarly gives marked febrile reactions.

Aniline dyes (mercurochrome, brilliant green, crystal violet) have been locally applied and injected intramuscularly. Severe toxic reactions with skin rashes and blood disorders were frequent, and the drugs were discarded. Thiamine only had one positive effect; it reduced nerve pain.

In 1940, diphtheria toxoid and antitoxin were acclaimed as specific against leprosy, but this was only a mistaken observation.

Sulfone drugs were first used in leprosy in 1941. Promin has been given to almost 200 patients at the Carville Leprosarium since that date, and the majority of these people had moderately to far advanced lepromatous leprosy. The results over these five years have been very encouraging, for almost all patients showed some improvement and about 40 per cent in one reported series had a reversal of the skin smear formerly positive for lepra bacilli. Advanced nodular lesions slowly resolved, and the patients noted a generalized improvement in themselves. The drug was described



as at least "the most beneficial of any drugs yet tried". Whether its action is chemotherapeutic is still a moot point. Toxic effects consist primarily of the production of anemia and more rarely skin rash. Because it proved to be too toxic when given orally, it has been injected intravenously. Diazone and promizole, two other sulfone drugs, have been given by mouth, and their effect on the disease was of about equal intensity to that of promin. The toxic effect was principally hemolytic anemia, occasionally skin eruptions and nausea and vomiting.

Several reports on promin and diazone from Latin America and Africa are quite as favorable as those from Carville.

Streptomycin has been begun on a small group of patients at Carville. No reports are yet available, but these patients have already shown some regression of lepromatous lesions.

#### CONCLUSION

Until 1941, only chaulmoogra oil had withstood the scrutiny of investigators sufficiently to be given the dubious title of the "most beneficial" agent known against leprosy. Since then, however, the sulfone drugs have, in the hands of several groups of leprologists, taken over this title. It now remains to be seen whether: (1) their action is specific against *lepra bacilli*; (2) they will cure early cases of leprosy; (3) other related compounds can be found whose effect is more pronounced and/or specifically chemotherapeutic; (4) streptomycin or another antibiotic yet to be discovered will be specific. It is certain that, though caution is necessary in ascribing antileprotic qualities to any drug, these recent developments of sulfones and antibiotics bring to the fore real possibilities that a true chemotherapeutic agent may soon be discovered.

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\*Because of the length of the list of references (290) it is impossible to publish it in toto. Any one interested in consulting the complete bibliography may do so at the office of the Journal.

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### FOOD CONSERVATION

The medical profession has been solicited to lend its support in the President's program to conserve food in our Country in order that the hungry and destitute people of Europe may be fed.

The prime problem and duty of the doctors is scientifically to assist and direct their patients and their families in trying to maintain a diet sufficient in calories and vitamins to sustain the individual in a healthy condition. The question of substitutions for the meatless Tuesdays and fowlless Thursdays will need the dietary assist-

ance of physicians and allied groups. Religious fasting and abstinence have accustomed most of our people to such a regime. Therefore to maintain this new order should not be such a difficult problem. We physicians should put forth the proper effort to assist in the successful handling of this regrettable emergency.

### STATE HOSPITAL SURVEY AND EXPANSION PROGRAM

In order to comply with the Hill-Burton Bill for survey and expansion of needed hospital facilities, the Governor of our State has caused to be set up a working committee to make a survey. This committee has been very busy for several months and it is understood that a tentative program has been perfected. The State Board of Institutions has been designated as the certifying agency for Louisiana. At a recent public meeting of interested agencies to hear objections to the proposed draft of plans, an inherent danger was brought forth. This is the possibility of establishment of a political bureaucracy in the state, which would control selection of the location, define the needs and supervise the expansion of privately owned hospitals as well as state institutions. It can well be understood what a distinct disadvantage would accrue if this is a fact and the injustice which would be inflicted upon physicians or lay people who own private hospitals and who would like to improve and expand their facilities by taking advantage of the provisions of the Hill-Burton Bill, and then have the disapproval of the certifying bureau, a political agency of the state. The great need for improvement in hospital and medical services should prompt the supplying of proper safeguards to prevent such from happening and thus assume an equitable supervision and assistance for these great humanitarian needs, free from any political strategy. It is hoped that the certifying agency will be conscious of such probable hardships and give their assurance to the end that same will be prevented.



## WE MUST BE VIGILANT

In the October issue of the *Journal* under the Organization Section there appeared an appraisal of the recent report of the Subcommittee of the Committee on Expenditures in the Executive Departments, House of Representatives, Forest A. Harness, Chairman. There were cited in this report six agencies or bureaus of the Federal Government which were alleged to have spent illegally federal funds for the promotion of "Health Workshops" in various places of the U. S. for the purpose of fighting for Federalization of Medicine. The same group of individuals who for years have been fighting for the Wagner-Murray-Dingell Eills, was again performing in these workshops by lending aid and their presence to these meetings. What an expose! It really lifted the iron curtain and exposed their activities. This same group of proponents of national health insurance, although having so far failed to reach their objective in this country, tried in every way to have a similar piece of legislation made into law in Hawaii. Thanks to a diligent and strong medical profession these plans back-fired and again failed. Do you think they ceased their efforts to promote government insurance? Not by any means. They proceeded to tighten up their belts and by alleged devious means secured a request for them to go to Japan as supposed Consultants to General MacArthur (without knowledge of Army officials) on health and medical expansion. From correspondence intercepted it was learned that their chief function was to establish governmental health insurance for Japan, a defeated and prostrate nation. They thus proposed to help reconstruction on a plan which is not now applicable to the United States. How ironical! Read what Representative Harness says in a letter to Representative John Faber, Chairman of Committee on Appro-

priations, House of Representatives, as follows:

"I deem it proper to bring this matter to your attention because it appears to me to involve a question of legislative policy for the consideration of the Appropriations Committee. All members of this mission are permanent full-time employees of the federal government and are well known in the United States for their persistent agitation for a national system of socialized medicine to be achieved through a program of compulsory health insurance. The members of the mission are:

"Joseph W. Mountain, Associate Chief, Bureau of States Services, U. S. Public Health Service; Burnet M. Davis, Surgeon, U. S. Health Service; Barkev S. Sanders, Chief, Health Studies Division, Bureau of Research and Statistics, Social Security Administration, and Frances A. Staten, Assistant Regional Director for Management, Federal Public Housing Authority.

"This mission departed for Tokyo on August 28, 1947. We are informed that at a later date the mission will be expanded to include Mr. Arthur J. Altmeyer, Commissioner of the Social Security Administration; Mr. Wilbur Cohen, Assistant Director of the Bureau of Research and Statistics, and possibly Mr. I. S. Falk, Director of the Bureau of Research and Statistics."

From this record we find the same groups, bureaus and individuals at work which have been so prominent in the past in supporting governmental insurance in our country. We must therefore continue to educate our physicians, members of Congress, and the public—how subtle and low these determined employees of the government will stoop to reach their goal. They have millions and the government behind them. We must develop courage and determination to press our cause, for right is might!

## ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

***An informed profession should be a wise one.***

### THE ACTIVITIES OF THE WASHINGTON OFFICE OF THE A.M.A.\*

JOS. A. LAWRENCE, M. D.†

For the director of the Washington Office, the day always begins with his scanning the morning papers—The Washington Post, before and during breakfast; and The New York Times, in the trolley, on his way to the office. The numerous news reporters, continually swarming through the Congressional halls and offices in their zealous search for news, uncover many doings and frequently discover early leads of actions contemplated by the Government divisions. The columnists' contributions must be scanned for references that may be made to proposed or pending health bills; also the column that reports what happened in Congress yesterday, and is to happen today, must be carefully read, and the names of the visitors who called on the president, noted. The morning mail which arrives at the office brings, in addition to correspondence, reports from two legislative reportorial services and the Congressional Record. Each in its way—and they differ somewhat in their fields of interest—will tell what happened "on the hill" the day before, and what the several calendars carry for today. We are particularly interested in learning whether any committees will hold hearings during the day on bills we are following and, if so, when they will begin and the rooms in which they will be held. The three legislative services report by title and number, the bills which were introduced in both houses the day before, and by whom sponsored. We study the list and check those to be followed and those to be read carefully. The same mail will bring printed copies of the bills introduced two days previously,

and such committee reports as were released by the Government Printing Bureau. We have a contract with the Bureau to send to the office a copy of every bill, report, or resolution as soon as it is printed.

After hastily scanning the mail, it is turned over to the director's assistant to study more carefully, while the director hurries to the Capitol or respective office building, to attend such hearing as may be scheduled. Hearings usually begin promptly at 10:00—occasionally one may be advanced to 9:30—and terminate at 12:00 noon, at which time the two Houses convene. If the hearing is a very important one and cannot be terminated by noon, the Chairman may ask permission of the respective House to continue during the afternoon. If permission is granted, it is with the understanding that the members will come to the Chamber if a roll call or vote is demanded.

In the afternoon, we take up our work in the office—attending to our correspondence, reading and studying the bills, resolutions and reports that were received. We must be prepared at all times—but particularly in the afternoons—to answer, with the proper information, such telephone calls as may come from the Congressmen or their secretaries (especially the secretaries of committees considering bills in which we are interested) for occasionally a Congressman will leave the chamber while a bill is being discussed and call us for some specific information that he may need for the debate. Some afternoons we call at the committee rooms and discuss with the secretaries our attitude on bills they are considering. We like to hear from the introducer of a health bill what he considers the special merits of the bill he is sponsoring and arrange to call upon him at his office in the morning before ten or in the afternoon, either in his office or by calling him from

\*Read before the Southern Regional Conference of the A.M.A., New Orleans, October 23, 1947.

†Director, Washington Office of the Council on Medical Service of the A.M.A.



the floor, as he may prefer. At their convenience, we call upon each member—beginning with the chairman—of the committees considering our bills, for the purpose of discussing the merits and scope of the several bills referred to them. These calls usually result in our being asked to provide them with specific information, relative to the professional aspects of the bills under discussion. We attend the sessions of the respective Houses when health bills are on the calendar for action.

Our attendance at hearings given health bills is very essential. Witnesses wishing to testify at hearings are required to submit to the clerk of the committee, several days in advance of the date set for the hearing, seventy-five written copies of their statements, in order that each member may have a copy to study in advance of the time it is presented. Extra copies are provided for distribution to the press, and others on the day of the hearing. These statements will all be printed eventually in the report of the hearings, but we immediately summarize each one or excerpt important paragraphs and report them in our bulletin, together with notes we collected while the hearing was in progress.

During the session, the office issues a bulletin at intervals of about ten days, in which is reported to a mailing list of over 1500 persons (mostly physicians) and organizations, the new bills introduced in the interval, such action as may have been taken on any bills previously reported, and the dates when hearings and conferences are to be held. Special bulletins are issued as necessary, in which are reported accounts of the hearings.

The Council has felt that there should be expressed in the bulletin, when important bills are reported, a statement of approval or disapproval, with explanatory reasons; and, at its request, the Board of Trustees has appointed a committee which will study each bill and instruct the director of the Washington Office as to the desirability of such legislation. These instructions will be promptly reported in the bulletin so that they may be used as a basis for conversa-

tion between a physician and his Congressmen.

In the office, a very careful file is kept for each bill reported in the bulletin. All correspondence relating to it and its subject matter, together with committee reports, newspaper clippings, and reports of discussions on the floor, are filed in one pocket and kept up to the minute. A cross index is maintained so that each bill is catalogued chronologically as introduced, as well as by subject and by name of introducer and sponsors. A file is also kept in which is recorded the name of each Congressman, his state, office number, names of committees or commissions of which he is a member, the bills he has introduced that interest us, and his announced attitude on health subjects. This information is also cross indexed, according to subject matter of bills introduced.

So much for Congress and its relations, but our work does not stop there. A more or less close relationship is maintained with all of the Government Departments and Bureaus that are engaged in administering the health and social security laws. The office receives regularly the newspaper releases and publicity material distributed by many of the Government departments, especially that issued by the Veterans' Administration, the Federal Security Agency, and the several branches of the U.S.P.H.S.

Government officials occasionally wish to discuss problems of medical care or public health with us.

Recently, representatives of the Civil Aeronautics Administration sought advice relative to revising the physical requirements demanded of applicants for a pilot's license. There is general agreement among the members of the Administration that an applicant for a license to fly commercially should pass a rigorous examination, but they are not agreed that an applicant who wishes to fly his own plane only should be required to pass the same examination, as one who aims to fly commercial planes. More time is required to learn to fly a plane than to operate an automobile and in this learning period physical weakness in the

applicant is likely to be discovered and reported by the pilot giving the lessons; hence, if a student is passed by his pilot, it may be assumed he can be considered physically fit at least to fly his own plane. No decision has been reached on this point as yet by the Commission.

The medical staffs of the Army, Navy and Veterans' Administration seek assistance in problems of public relations arising from their contacts with civilian members of the profession. A most annoying problem before the Veterans' Administration at present is—how to guarantee the veterans topnotch care in those states where chiropractors are licensed and insist upon being included in the treatment program.

This problem is most complicated in eleven states, where schools teaching chiropractic have been approved by the proper authorities for cooperation in the Veterans' Education Program. Not one of these schools, so far as we are informed, is a part of any recognized educational institution. They are all commercially conducted. However, approval by the state's agency gives them a status which will justify their graduates in seeking licensure to practice in the state, and also authority to partake in the Government program for providing medical care for veterans. It will be very difficult, because of the emotional aspect, for other states, where chiropractors are not licensed to practice, to deny these veterans the right to practice in their jurisdictions, if they seek it. Chiropractic seems to have achieved a legal status without scientific justification.

Leading labor unions have their headquarters in Washington, and we have been invited to conferences when they have medical matters under consideration. Just recently we have assisted Doctor Martin, of the Council on Medical Service, in arranging conferences with representatives of the United Mine Workers Union regarding improvement in the medical service rendered miners in the bituminous coal region.

Senator Byrd, several years ago, conducted a survey of the Government Departments, Bureaus and Agencies and reported

finding thirty-four of them carrying, in their annual budgets, some appropriation for health work. Since then, a few have abandoned their health activities but most persist. We are gradually informing ourselves of the activities conducted with those various funds.

The Congress, this year, authorized the appointment of a Commission to make an investigation of the various bureaus, divisions and agencies of the Executive Department of the Government, for the purpose of ascertaining the extent to which overlapping of funds and activities occur and, within the last month, Pres. Truman has announced the personnel of the Commission. It is to be headed by Ex-President Hoover, who has temporarily established his residence in Washington so as to give the work his full attention.

The correspondence of the office is very heavy during the time the Congress is in session. We have many inquiries from state, county and auxiliary society legislative chairmen for information concerning reported bills and for copies of bills or reports. Communications, in the form of suggestions and requests for information or material, are very welcome and with rare exception acknowledged and supplied on the day received. Also, answering the telephone calls, both local and long distance, absorbs a good part of every day.

Physicians visiting Washington usually call at the office either to visit or for assistance. Physicians are invited to make it their headquarters and avail themselves of its facilities.

The Washington Office aims to be a source of information and a liaison between the Congress and the profession; and, in order to accomplish this aim, it was deemed wise to register under the Lobbying Act. There are more than twenty agencies and individuals registered under the Act as interested in legislation relating to health activities. This is not the largest lobby, but it is significant of the interest health legislation commands throughout the country. Most of these representatives have established permanent offices in the city.



And now—a word with regard to the legislation we are following. Of the 7,289 (2108 S.—5181 H. R.) bills and resolutions introduced in the two Houses of this, the 80th Congress, 132 (51 S.—81 H. R.) were selected as of interest to our profession. Of this number, only fifty-six were advanced to the stage of hearings, and forty of these were reported out of committee to their respective chambers for passage, of which eight were passed by both Houses and have become a part of our Public Laws except for one (S. 526) which was vetoed by the President. Those not acted upon, either by the reference committees or by the respective Houses, may be taken up by the Congress when it reconvenes in January.

A bill (S. 140) which would create a Department of Health, Education and Security with Cabinet stature reached the floor of the Senate, but was not debated before the Senate recessed. This bill, after further amendment, may be enacted. Hearings were in progress on the Senate side, on the two medical service bills (S. 545—S. 1320). They will be concluded in the next session and the committee will decide upon some course of action in their regard. Several

other highly socialistic bills demanding our very close watch are:

S. 1679—Broaden Social Security—Murray.

S. 1714—Maternal and Child Health Services—Pepper.

S. 1734—Unemployment Cash Sick Benefits—Murray.

H. R. 1980—Medical Care for School Children—Howell.

The 64 dollar question is: Will this Congress pass a compulsory health insurance bill? Your guess is probably as good as any other, but it can be safely said that it will not pass any of the present bills in the form they are now.

Adequate medical care is of such undisputed importance that Congressmen will consider any plan that promises to make it more available to the entire population. The feeling seems to be extending that if voluntary prepayment plans can do the work, they should be given the opportunity. At any rate, there seems to be unanimous agreement that any medical service plan will function best when organized on a state or community basis.

## LOUISIANA STATE MEDICAL SOCIETY NEWS

### C A L E N D A R

#### PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

#### SECOND DISTRICT MEDICAL SOCIETY

On Thursday, October 16 a group of New Orleans physicians who have participated in programs of the Second District Medical Society and have been honored by that group, were hosts to members of the District Society and their wives at a dinner at Antoine's. All present had a most enjoyable time and it is felt that Dr. Edmund Connelly, who arranged for the dinner, and Dr. J. T. O'Ferrall, who presided on the occasion, should be

congratulated on the pleasant evening furnished. Similar dinners have been given in past years and by the interest manifested should be continued in the future.

#### SEVENTH DISTRICT MEDICAL SOCIETY

On September 20 the annual fall conference of the medical society of the Seventh Congressional District was held in Lake Charles. The program for this conference was outstanding with such men

as Dr. Walter Grady Reddick, Dr. O. B. Gober, Dr. Hampton C. Robinson, Dr. Arild E. Hansen, and Dr. Marvin P. Knight, all of Texas, participating. In addition Dr. Champ Lyons spoke on "Management of Thermal Burns", Dr. Richard W. Vincent on "Plastic Surgery in Treatment of Burns", Dr. Joseph S. D'Antoni on "Diagnosis and Treatment of Amebiasis", Dr. John Adriani on "Obstetrical Anesthesia with Special Emphasis on Saddle and Spinal Anesthesia" and Dr. Conrad G. Collins on "Ovarian Pathology and Indications for Surgical Intervention". The meeting was presided over by Dr. J. J. Stagg, Jr., President of the Seventh District Society and Dr. J. Y. Garber, President of the Calcasieu Parish Medical Society, extended greetings to members and guests present.

At an informal dinner held at the Lake Charles Country Club Dr. Gilbert C. Anderson, President of the State Society, gave an address and brief talks were made by Dr. P. H. Jones, First Vice-President of the State Society, and Dr. Claude Martin, Councilor of the Seventh District.

The committees on arrangement for this meeting are indeed to be commended for the excellent program planned. It is very seldom that so many outstanding speakers are secured for a one day meeting and it is felt that all in attendance profited a great deal from a scientific standpoint and had a most enjoyable time socially.

It would no doubt be well for other district societies in the state to follow the example set by the Seventh District Society in having an annual conference of this type.

#### LAFOURCHE VALLEY MEDICAL SOCIETY

A meeting of the Lafourche Valley Medical Society was held at Grand Isle on September 13 and 14. This meeting included a scientific program, a dinner and other social activities and was greatly enjoyed by all present. It is hoped that the doctors of this section who failed to attend will be able to do so when another such opportunity is presented.

#### WASHINGTON PARISH MEDICAL SOCIETY

The Washington Parish Medical Society was recently reorganized at a meeting held for this purpose in Bogalusa. Dr. R. R. Ward was elected president of the group, Dr. R. D. Fornea, vice-president and Dr. C. W. Crain, secretary.

#### WEBSTER PARISH MEDICAL SOCIETY

At a meeting of the Webster Parish Medical Society, held in Minden on September 30, Dr. C. R. Reed, Jr., of Shreveport, gave a talk on "Diagnosis and Treatment of Cervical Fractures and Dislocations". Dr. J. P. Sanders, also of Shreveport, addressed the group outlining the aims and purposes of the American Academy of General Practice.

#### PARISH MEETINGS OF LOUISIANA FARM BUREAU

Members of the State Society are urged to attend meetings which are called by the Louisiana Farm Bureau in various parishes throughout the state for discussion of medical service for rural areas. Our cooperation has been requested and unless physicians are alert and actively interested in this subject there may be an attempt by some agencies toward socialization of this type of practice.

#### BURCH TO HEAD TULANE DEPARTMENT OF MEDICINE

Dr. George Edward Burch, associate professor of clinical and experimental medicine in the School of Medicine at Tulane University, has been appointed Chairman of the Department of Medicine and professor of medicine at the University, to succeed Dr. John H. Musser who served as head of the Tulane Medical Department for the past 23 years.

Dr. Burch is a native of Edgard, Louisiana and graduated from the Tulane Medical School in 1933 receiving his Master of Science degree from the University in 1934. In 1935 he was appointed instructor of medicine at Tulane and was named associate professor of medicine in 1943.

Research in the use of radio-active tracers in heart diseases earned for Dr. Burch the American Medical Association's gold medal award for the most original exhibit at the annual meeting held in Atlantic City last June. The exhibit illustrated the use of radio-active sodium in the study of congestive heart failure.

Formerly on the staff of the hospital of the Rockefeller Institute for Medical Research and consultant in medicine (cardiovascular) to the Surgeon General of the United States Army, Dr. Burch is at present senior visiting physician at Touro Infirmary and Charity Hospital in New Orleans. He is also consultant in cardiovascular diseases at Ochsner Clinic.

The Louisiana State Medical Society wishes to extend to the Tulane University and to Dr. Burch its felicitations on this appointment.

Dr. Roy Carl Young, of Covington, presented a paper on "Clinical Observations on the Treatment of the Alcoholic" at the Southern Psychiatric Association Meeting in Birmingham, on October 13 and 14.

#### SOUTHERN MEDICAL ASSOCIATION MEETING

The 1947 meeting of the Southern Medical Association to be held in Baltimore November 24-26 will no doubt be one of the most interesting and profitable meetings held by this organization. The meeting this year will be concentrated into three



days instead of three and one-half. Registration will open Monday morning, November 24 and the scientific program for that day will be conducted by the local profession. Meetings of the 21 sections of the Association will be held on Tuesday and Wednesday, November 25 and 26. Following is synopsis of the clinical sessions and sections for this meeting:

Monday, November 24. Forenoon and afternoon—General Clinical Sessions, Baltimore Day, medicine, surgery, and ophthalmology and otolaryngology, presentations by physicians of Baltimore. A General Public Session will be held at the Lyric Theater on Monday evening.

Tuesday, November 25. Forenoon—Section on Gastroenterology, Section in Neurology and Psychiatry, Section on Orthopedic and Traumatic Surgery, Section on Urology, Section on Industrial Medicine and Surgery, and Section on Medical Education. Afternoon—Section on Medicine, Section on Ophthalmology and Otolaryngology, Section on Surgery, Section on Obstetrics, Section on Physical Medicine, and Section on Public Health. A General Public Session featuring the address of the President followed by the President's Reception and Ball will be at the Lord Baltimore Hotel on Tuesday evening.

Wednesday, November 26. Forenoon—Section on Pediatrics, Section on Dermatology, Section on Radiology, Section on Gynecology, and Section on Anesthesiology. Afternoon—Section on General Practice, Section on Allergy, Section on Pathology, Section on Proctology, and Section on Ophthalmology and Otolaryngology.

#### ALLERGISTS TO MEET

The American Academy of Allergy will hold its annual convention at Hotel Jefferson, St. Louis, Missouri, December 15-17 inclusive. All physicians interested in allergic problems are cordially invited to attend the sessions as guests of the Academy by registering without payment of fee. The program, the scientific and technical exhibits have been arranged to cover a wide variety of conditions where allergic factors may be important. Papers will be presented dealing with the latest methods of diagnosis and treatment as well as the results of investigation and research. Round table conferences will be held on Monday afternoon, December 15. Advance copies of the program may be obtained by writing to the Chairman on Arrangements, Charles H. Eyermann, M. D., 634 North Grand Boulevard, St. Louis, Missouri.

#### RADIOLOGICAL SOCIETY OF NORTH AMERICA

The thirty-third annual meeting of the Radiological Society of North America will be held at the Hotel Statler in Boston, November 30-December 5. The meeting will open with registration on Sunday and the general session on Monday will include a

symposium on the Economics of Medicine. Numerous papers pertaining to the latest advances in x-ray diagnosis and treatment will be delivered by members of the society each afternoon. On Wednesday morning symposia on pediatric roentgenology and on radioactive iodine, which is used in the treatment of certain thyroid conditions, will be held.

#### AMERICAN COLLEGE OF SURGEONS

The following members of the Louisiana State Medical Society were accepted into fellowship of the American College of Surgeons at the thirty-third convocation of the College held in New York on September 12: Drs. John A. Colclough, Daniel W. Goldman, Alfred B. Longacre, Melvin D. Steiner and Max Suter; all of New Orleans.

#### HOMETOWN MEDICAL CARE PLAN FOR VETERANS

On November 6, just preceding the secretaries and editors conference in Chicago there will be held by the A. M. A. a session for discussion of the Hometown Medical Care Plan for Veterans at present in effect in many states. At this meeting will be considered the questions of How is the plan working?; What are the difficult problems involved?; and Where and why should changes be made in the program?

#### AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC.

The next written examination (Part I) for all candidates will be held in various cities of the United States and Canada on Friday, February 6, 1948 at 2:00 p. m. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination held later in the year.

A number of changes in Board regulations and requirements were put into effect at the last annual meeting of the Board held in Pittsburgh, Pennsylvania, from June 1 to June 7, 1947. Among these is the new ruling that the Board does not subscribe to any hospital or medical school rule that certification is to be required for medical appointments in ranks lower than Chief or Senior Staff of hospitals, or Associate Professorship in Schools of Medicine, for the obvious reason that such appointments constitute desirable specialist training. At this meeting the Board also ruled that credit for graduate courses in the basic sciences which involve laboratory and didactic teaching rather than clinical experience or opportunities will be given credit for the time spent up to a maximum period of not more than six months regardless of the duration of the course.

Applications are now being received for the 1948 examinations. Closing date for these applications will be November 1, 1947.

For further information and application blanks

address: Paul Titus, M. D., Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

### INFORMATION NEEDED FOR A. M. A. DIRECTORY

Preparations are now being made to publish the new, Eighteenth Edition of the American Medical Directory. The last edition of the Directory was issued late in 1942. Since that time, it has been impossible to publish a new edition because of wartime restrictions and the shortage of paper and labor.

About November 15, a directory card will be mailed to every physician in the United States, its dependencies, and Canada, requesting information to be used in compiling the new Directory. Physicians receiving an information card should fill it out and return it promptly whether or not any change has occurred in any of the points on which information is requested. It is urged that those physicians also fill out the right half of the card, which information will be used exclusively for statistical purposes. Even if a physician has sent in similar information recently, mail the card promptly to insure the accurate listing of his name and address. There is no charge for publishing the data nor are physicians obligated in any way.

The Directory is one of the most important contributions of the American Medical Association to the work of the medical profession in the United States. In it, as in no other published directory, one may find dependable data concerning physicians, hospitals, medical organizations and activities. It provides full information on medical schools, specialization in the fields of medical practice, memberships in special medical societies, tabulation of medical journals and libraries, and, indeed, practically every important fact concerning the medical profession in which anyone might possibly be interested.

Therefore, should any physician fail to receive one of these Directory Information cards by December 1, he should write at once to the Directory Department requesting a duplicate card be mailed.

### PRESENT DEMAND FOR NURSES

The American Nurses' Association has recently issued a statement concerning the present shortage of nurses and has proposed a program to attempt to remedy this situation. The Association "with all its resources, pledges itself to work to the limit in initiating and furthering activities to cope with this situation", according to the statement. It is gratifying to know of this activity and also to know that a special committee from the American Medical Association has been appointed to consider this subject. With such combined efforts it is hoped that this crisis may be relieved.

### MOTION PICTURE FILMS

To assure the listing of all outstanding medical and surgical motion picture films in the revised "Catalogue of Professional Motion Picture Films" now being compiled by the Academy-International of Medicine, all film authors are urgently requested to write immediately for film questionnaires to be filled out and returned. Such requests should be addressed to the Academy-International of Medicine, 214 West Sixth Street, Topeka, Kansas.

### MARKLE FOUNDATION POST-FELLOWSHIP GRANTS

Two hundred and fifty thousand dollars has been made available annually for five-year post-fellowship grants beginning 1948-49 by the John and Mary R. Markle Foundation. The purpose of the program is to attract much-needed talent to academic medicine by giving promising young scientists academic security and financial assistance for a period up to five years. The program will be conducted in cooperation with accredited medical schools in the United States and Canada and further details may be secured from the deans of such schools.

### BENEFIT SHOE FOUNDATION

The Bristol Manufacturing Corporation, through its department of Christian Relations, has begun operation of the Benefit Shoe Foundation. This is a non-profit corporation offering single shoes and odd pairs at cost for amputees, paraplegics and others with mismated feet. For further information communicate with the National Foundation for Infantile Paralysis, 120 Broadway, New York City.

### LESLIE DANA MEDAL

The award made annually for outstanding achievements in the prevention of blindness and the conservation of vision, by the National Society for the Prevention of Blindness, will be presented this year to Dr. Frederick H. Verhoeff, of Boston.

### NATIONAL GASTROENTEROLOGICAL ASSOCIATION 1948 AWARD CONTEST

The National Gastroenterological Association has announced its Annual Cash Prize Award Contest for 1948. One hundred dollars and a Certificate of Merit will be given for the best unpublished contribution on gastroenterology or allied subjects. Certificates will also be awarded those physicians whose contributions are deemed worthy.

Contestants residing in the United States must be members of the American Medical Association. Those residing in foreign countries must be members of a similar organization in their own country. The winning contribution will be selected by a board of impartial judges and the award is to be



made at the Annual Convention Banquet of the National Gastroenterological Association in June of 1948.

Certificates awarded to other physicians will be mailed to them. The decision of the judges will be final. The Association reserves the exclusive right of publishing the winning contribution, and those receiving certificates of merit, in its official publication, *Review of Gastroenterology*.

All entries for the 1948 prize should be limited to 5,000 words, be typewritten in English, prepared in manuscript form, submitted in five copies, accompanied by an entry letter, and must be received not later than April 1, 1948. Entries should be addressed to the National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.

#### UROLOGY AWARD

The American Urological Association offers an annual award of \$1000.00 (first prize of \$500.00, second prize \$300.00 and third prize \$200.00) for essays on the result of some clinical or laboratory research in urology. Competition shall be limited to urologists who have been in such specific practice for not more than five years and to residents in urology in recognized hospitals.

The first prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Hotel Statler, Boston, Massachusetts, May 17-20, 1948.

For full particulars write the Secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis, Tennessee. Essays must be in his hands before March 1, 1948.

#### ALVARENGA AWARD

In recognition of his studies on the evaluation of BCG vaccine in the control of tuberculosis the College of Physicians awarded on July 14, the Alvarenga Prize for this year to Dr. Joseph Aronson, of the United States Bureau of Indian Affairs.

The Alvarenga Prize was established by the will of Pedro Francisco daCosta Alvarenga of Lisbon, Portugal, an Associate Fellow of the College of Physicians, to be awarded annually by the College of Physicians on each anniversary of the death of the testator, July 14, 1883.

The College usually makes this award for outstanding work and invites the recipient to deliver an Alvarenga Lecture before the College.

#### ANNOUNCEMENT OF VAN METER PRIZE AWARD

The American Association for the Study of Goiter again offers the Van Meter Prize Award of Three Hundred Dollars and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. The Award will be made at the annual meeting of the Association which will be held in

Toronto, Canada, May 6th, 7th, 8th, 1948 providing essays of sufficient merit are presented in competition.

The competing essays may cover either clinical or research investigations; should not exceed three thousand words in length; must be presented in English; and a typewritten double spaced copy sent to the corresponding secretary, Dr. T. C. Davison, 207 Doctors Building, Atlanta 3, Georgia not later than February 1st, 1948. The committee, who will review the manuscripts, is composed of men well qualified to judge the merits of the competing essays.

A place will be reserved on the program of the annual meeting for presentation of the Prize Award Essay by the author if it is possible for him to attend. The essay will be published in the annual Proceedings of the Association. This will not prevent its further publication, however, in any Journal selected by the author.

#### CANCER CONFERENCE

The Southwest Regional Cancer Conference will be held in Fort Worth on November 20 at the Blackstone Hotel. This conference will be held under the auspices of the American Cancer Society and in cooperation with the Texas Division of the American Cancer Society. The one-day meeting will consist of morning and afternoon lecture sessions followed by open forum question and answer periods, a clinical luncheon and a public meeting in the evening. Further information about the conference may be secured from the Tarrant County Medical Society, 209 Medical Arts Building, Fort Worth 2.

#### HEALTH OF NEW ORLEANS

The Bureau of the Census, Department of Commerce, from the figures reported by the New Orleans Health Department, announces that there were reported in the City of New Orleans 133 deaths during the week which ended September 6. Eighty-eight of these deaths occurred in the white population and 45 in the negro with 19 in children under one year of age; 14 colored and five white. An increase in number of deaths reported is noted for the week which ended September 13. There were 97 white people who expired this week and 65 colored, six of the former and seven of the latter occurring in infants under one year of age. The report for the week ending September 20 showed a slight decrease in the total number of deaths, this being 153, divided 101 white and 52 nonwhite. The infant deaths, however, increased to 26, an equal number occurring in the white and colored. There were 59 fewer people who died in the city during the week ending September 27 than for the previous week; 58 white and 36 colored and only ten of these occurred in infants. The report for October 4 showed a total of 111 deaths including 13 infant deaths.

## INFECTIOUS DISEASES IN LOUISIANA

The weekly morbidity report for the State of Louisiana for the week ending August 30 indicated that there were 46 new cases of cancer occurring in the state this week. The only other diseases reported in numbers greater than ten were pulmonary tuberculosis with 27 cases and unclassified pneumonia with 24. Meningococcus meningitis occurred in one instance in Vermilion Parish and there was one case of poliomyelitis reported from St. Martin Parish. Pulmonary tuberculosis led other reported diseases in incidence the next week as shown by the report for the week ending September 6. There were 78 cases of this disease reported followed by 30 cases of cancer, 23 each of malaria and unclassified pneumonia, 11 cases of whooping cough and 10 cases of septic sore throat. Twenty-two of the malaria cases occurred in Jackson Parish and one in Orleans. One case of poliomyelitis was reported from Lafourche Parish. There was a decrease in number of pulmonary tuberculosis cases reported for the week ending September 13, there being 60 listed. This was closely followed by 59 cases of cancer. Whooping cough with 15 cases, unclassified pneumonia with 12 and measles with 10, were the only other diseases reported in numbers of ten or more. There were no cases of poliomyelitis reported this particular week, however one case of meningococcus meningitis occurred in Orleans Parish and one in Webster Parish. Cancer and pulmonary tuberculosis were still the most prevalent diseases in the state according to the report of September 20. There were 30 cases of cancer and 13 of pulmonary tuberculosis reported this week and no other diseases were reported in numbers larger than ten. Two cases of meningococcus meningitis were reported; one from Franklin and one from Orleans Parish.

MONTHLY MORBIDITY FOR VENEREAL  
DISEASES

## STATE OF LOUISIANA

Month Ending August 31, 1947

	Total This Month	Total Previous Months	Total to Date 1947
Chancroid	61	372	433
Gonorrhea	1276	8764	10040
Granuloma Inguinale	18	123	141
Lymphopathia Venereum	8	54	62
Syphilis	922	6757	7679

WOMAN'S AUXILIARY, LOUISIANA STATE  
MEDICAL SOCIETY

Honor was conferred on the Woman's Auxiliary to the Louisiana State Medical Society when at the annual meeting of the Woman's Auxiliary to the American Medical Association held in Atlantic City, June 9-12, Mrs. Arthur A. Herold of Shreveport, was elected and installed as Treasurer for

the year 1947-48. Mrs. Herold has a most enviable record for length of service to the Woman's Auxiliary. She has held the following chairmanships: legislative chairman for four years, 1931-1932, and 1938-1941; director for three years, 1934-1936, and 1946-1947, resigning as director for 1947-1948 to accept the arduous duties of the office of treasurer; constitutional secretary, 1944-1946, being the first member to serve in this office under the new constitution and by-laws; and chairman of the resolutions committee, 1941-1942. Mrs. Herold has served as a member of many committees during the time that she has been a member of the Board of Directors and has attended annual meetings, conferences and Board meetings regularly.

Mrs. Herold has been an active member of the Woman's Auxiliary for many years. She was president of the Caddo Parish Auxiliary in 1928, and organized the Woman's Auxiliary to the Louisiana State Medical Society in 1929, serving first as its vice-president and the following year as president. She has been active in both her parish and state auxiliaries since that time. In 1933-1934, Mrs. Herold was president of the Woman's Auxiliary to the Southern Medical Association.

Mrs. Herold has held various offices in civic, educational and philanthropic organizations, and during the war was chairman of the Home Front Committee of the O. C. D. in Shreveport and of a Surgical Dressing group of the Red Cross. She has been president of the Woman's Department Club of Shreveport and has served as legislative chairman of the state and local branches of the American Association of University Women. For three years she has been Commander of the Field Army of the American Cancer Society, Caddo Parish.

We congratulate the Auxiliary to the American Medical Association for having a woman of Mrs. Herold's ability to serve as treasurer. Mrs. Herold is very highly regarded for her accomplishments and greatly loved for her gracious and charming personality by our State Auxiliary.

Mrs. Herold recommends two books that won the Norton Medical Award and should be of special interest to the wives of physicians: THE DOCTOR'S JOB—1945 by Carl Binger, M. D., and A SURGEON'S DOMAIN—1947 by Bertram M. Bernheim, M. D. The Norton Medical Award was established to encourage the writing of books for laymen by physicians or other professional workers.

## CORRECTION

In the list of officers of the Woman's Auxiliary, carried in the October issue of the Journal the address of the Third Vice-President, Mrs. J. Eugene Toups was listed as 1956 Cloverdale Ave., Shreveport. The street address is correct, however the city should have been Baton Rouge.



## BOOK REVIEWS

*Roentgen Interpretation*: By George W. Holmes, M. D. and Lawrence L. Robbins, M. D. 7th ed. rev. Philadelphia, Lea and Febiger, 1947. Pp. 398. Price, \$7.00.

This is the seventh edition of an excellent text which has retained its position as the outstanding concise and comprehensive work on roentgen interpretation since the first edition in 1919. There are very few radiologists and teachers of radiology who are not thoroughly familiar with the book.

Dr. Lawrence Robbins has replaced Dr. Ruggles and the authors have attempted to keep the character of the book unchanged. This edition represents the first step in the gradual replacement of the positive prints of previous editions by negative illustrations. The subject matter has been thoroughly revised and brought up to date.

The text consists of an introduction and eleven chapters.

Chapter I deals with the many shadows and artefacts, which may cause confusion in interpretation. Of equal importance and as capably handled is the text of the second chapter pertaining to anatomical variations and development.

Chapter III on fractures and dislocations is of necessity short but the most frequent types of fractures are covered. Chapter IV is devoted to diseases of bone, Chapter V to the skull, Chapter VI to the spine and Chapter VII to joints, tendons and bursae. The chest, gastro-intestinal and genito-urinary tracts are discussed in Chapters VIII, IX and X respectively.

The last chapter on fluoroscopy, is especially valuable with the increased use of this diagnostic method. The statements regarding protection in fluoroscopy are timely and should be recognized as important by all who attempt this procedure.

As in the previous editions the text is clear and concise and in spite of its brevity the fundamentals of roentgen diagnosis are covered. The selection of illustrative roentgenograms is very good.

J. N. ANÉ, M. D.

*A Manual of Otology, Rhinology and Laryngology*:

By Howard Charles Ballenger, M. D., F. A. C. S. 3rd ed. enl. and rev. Philadelphia, Lea & Febiger, 1947. Pp. 352, illus. pl. Price, \$4.50.

This is one of the latest of many manuals on this subject. In three hundred and forty-six pages, 135 illustrations and 3 color prints the author has given a very concise and comprehensive brief of the subject. The book seems well suited for residents and those wanting a manual of disease and treatment of the ear, nose and throat.

Therapy is especially good, being up to date, concise and practical, something many of the other books have lacked.

The chapters dealing with hay fever and al-

lergy and that on headaches and neuralgias are very good and form a comprehensive working basis in dealing with these conditions.

The section on diseases of the ear brings up to date and in concise form a subject that is more or less at the cross roads in this day of chemotherapy.

This manual is well recommended as a reference book for otolaryngological residents, post-graduate students and as a modern reference in the office.

MERCER G. LYNCH, M. D.

*Histopathology of the Ear, Nose and Throat*: By Andrew A. Eggston, B. S., M. D. and Dorothy Wolff, A. B., M. A. Ph. D. Baltimore, The Williams & Wilkins Co., 1947. Pp. 1080, illus. pl. Price, \$18.00.

This is a welcome book to the otolaryngologist. For many years there has been talk of the need of such a book and rightly so for few textbooks of pathology give much time or space to ear, nose and throat pathology. In this book of 1080 pages beautifully illustrated, the authors have comprehensively covered the subject matter in a style which makes for easy reading. The illustrations are well grouped and spaced, as to be easily referred to, and very clear in their descriptions.

This is a book well recommended as an adjunct to every otolaryngologist's library, as well as that of the general pathologist. This is the first book of its kind to be published and marks another milestone in the progress of this specialty.

MERCER G. LYNCH, M. D.

*The Pharmacopoeia of the United States of America*: Thirteenth Revision (U. S. P. XIII). Easton, Pennsylvania, Mack Publishing Company, 1947. Pp. 957, illus. Price, \$8.00.

The thirteenth revision of the Pharmacopoeia of the United States which became official April 1, 1947, marks another milestone in the history of this publication which first appeared in 1820. Although the pharmacopoeia is more widely circulated in the profession of pharmacy than among physicians, the latter receive no small benefit from the labor involved in each new edition. The drugs admitted to the pharmacopoeia are therapeutic agents which reflect the best medical knowledge of the day. Their choice involves the retaining of time-tested remedies of previous revisions or their replacement by more effective agents which have been adequately tested from the standpoint of therapeutic action and safety. With the rapid advances in therapy on the one hand and the plethora of new drugs and preparations on the other the pharmacopoeia is of value to the physician as a guide for the wise selection of therapeutic

agents. The pharmacopoeia is legally authorized to designate standards of potency and properties of the included preparations, a service which is usually taken for granted by those prescribing and using drugs. The regular revisions are now appearing at five year rather than at ten year intervals which was formerly the case. Furthermore in order to keep in step with recent rapid developments it has been necessary to adopt a continuous revision by issuing supplements as occasion requires.

The general character of the information supplied by the pharmacopoeia is essentially the same as in the past. It is not a text on pharmacology or therapeutics in that no discussion of the action or therapeutic application of the drugs are included. A description of the physical and chemical properties of the drug is given with methods of identification and assay. An average dosage is also included. Many preparations found in U. S. P. XII do not appear in U. S. P. XIII among which may be mentioned bismuth subnitrate, carbon tetrachloride, ergot and the fluid extract of ergot, reduced iron, mercuric bichloride, mercury with chalk, a number of the volatile oils, phenyl salicylate and sulfapyridine. On the other hand a lengthy list of drugs are included for the first time such as carbachol, digitoxin, helium, protamine zinc insulin injection, lanatoside C, metacholine chloride, papaverine hydrochloride, sulfamerazine and various preparations of penicillin. A further noteworthy change in this revision may also be mentioned. English titles of drugs occupy the leading position and determine the alphabetical arrangement, with the previous Latin titles relegated to a secondary position. The alphabetical arrangement also involves the grouping together of various preparations—(tinctures, emulsions, etc.), and dosage forms (capsules, tablets, injections, etc.) of the same drug, in contrast to their appearance at widely separated points in U. S. P. XII.

This new revision of the Pharmacopoeia of the United States definitely merits the attention of all those who prescribe drugs.

RALPH G. SMITH M. D.

*Practical Emulsions*: By H. Bennett. 2d ed. rev. Brooklyn, N. Y., Chemical Publishing Co., Inc., 1947. Pp. 568. Price, \$8.50.

In this book emulsions are considered from the standpoint of the practical worker in contrast to theoretical treatises on the colloid and physico-chemical aspects of the subject. The first part of the book is concerned with general information

such as types of emulsions, emulsifying agents, methods of preparation and modern equipment. Chapters on stability and dispersing and wetting agents are also included. In this section of the book will be found a certain amount of theoretical as well as practical information on the above phases of the subject. The second section which is an innovation in this edition consists of a symposium on industrial emulsions written by authorities in various fields. Papers on lecithin, pectin, polyhydric alcohols and soaps as emulsifying agents are included. Of interest to the physician is a paper by Abraham Taub on surface active agents as germicides which deals with the action of such cationic agents as Zephiran Chloride, Phermerol and Ceepryn. It was of interest to the reviewer to learn that Domagk who was awarded the Nobel prize for his work on or in sulfonamides also initiated the technical development of these cationic agents as germicides. A further chapter in this section includes papers on cosmetics, dyes, paints, leather goods, foods, industrial waxes and synthetic rubber latex in many preparations of which emulsion formation is of primary importance. The third and most extensive part of the book consists of formulae for emulsions with brief directions for their preparation. These are classified by chapters according to use such as agricultural sprays, cleaners and soaps, cosmetics and drugs, food emulsions, medical emulsions, paints, polishes, etc. It is obvious that this book is of primary interest to those who are concerned with the manufacture or practical aspects of emulsions. From the standpoint of the physician the information with certain minor exceptions must be classified as "cultural."

RALPH G. SMITH, M. D.

#### PUBLICATIONS RECEIVED

The Commonwealth Fund, New York: *The Practical Nurse*, by Dorothy Deming, R. N.

J. B. Lippincott Company, Philadelphia: *Handbook of Psychiatry*, by Winfred Overholser, A. B., M. D., Sc. D. and Winifred V. Richmond, B. S., A. M., Ph. D.

C. V. Mosby Company, St. Louis: *Synopsis of Obstetrics* (3rd edition), by Jennings C. Litzenberg, B. Sc., M. D., F. A. C. S.; *Communicable Diseases* (2nd edition), by Franklin H. Top, A. B., M. D., M. P. H., F. A. C. P.

Grune & Stratton, New York: *Epilepsy*, by Paul H. Hoch, M. D. and Robert P. Knight, M. D.

Charles C. Thomas, Springfield, Illinois: *Trichomonas Vaginalis and Trichomoniasis*, by Ray E. Trussell, M. D.



# New Orleans Medical

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### AIRBLOCK IN THE NEWBORN PERIOD\*

GEORGE W. SALMON, M. D.†

HOUSTON, TEXAS

#### INTRODUCTION

In recent years there has been a great deal of interest in the efficiency of the lung as an air container. It has become apparent that air may escape from the respiratory passageways in a wide variety of conditions in all age groups.<sup>1</sup> The resulting clinical syndrome has been termed airblock.<sup>2</sup> I have been particularly interested in this problem as it applies to the newborn period.

On large newborn services it is a well-appreciated observation that in a high proportion of the deaths the cause of the fatal outcome may not be discovered at autopsy. All too frequently the death is attributed to small areas of atelectasis, although it is well known that normally the lungs may require several days or more completely to expand; to intracranial hemorrhage of insignificant size; to "immaturity"; to an enlarged thymus; or to other causes of questionable importance. The purpose of the investigation of my colleagues and myself<sup>3, 4</sup> has been to determine if airblock might be a factor in some of these deaths: either alone in severe cases, or in less severe instances in conjunction with other factors

which of themselves might not have led to a fatal outcome. It should be stated here that small amounts of aberrant air may cause little harm and produce no symptoms.

There are two good reasons for believing that aberrant air is frequently unappreciated at necropsy. The first is that it may be easily overlooked. Pneumothorax may not be detected unless particularly sought for. Although emphysema in the anterior mediastinum is readily detected, in the posterior mediastinum it is easily missed. Pulmonary interstitial emphysema may pass unrecognized or be thought an artefact. If the lung is fixed by immersion of small blocks of tissue, the air may be forced out by shrinkage caused by the fixative. The second reason is that it has been demonstrated clinically that aberrant air is not uncommon: one variety, pneumothorax, occurs in approximately one per cent of newborn infants.<sup>5</sup> Regardless of the cause of death, pneumothorax might be expected to be present in one per cent of newborn deaths. Moreover, if pneumothorax is ever deleterious in itself, it might be expected to be present in more than one per cent. Such an incidence of pneumothorax suggests that other varieties of aberrant air may not be unusual. These two reasons seem to warrant the inclusion of efforts to detect aberrant air as a part of the routine postmortem examination of newborn infants.

#### ETIOLOGY

Both experimental<sup>2</sup> the clinical<sup>4, 6</sup> evidence indicates that the escape of air from the respiratory passageways is in the lung itself. Pulmonary interstitial emphysema

\*Read before the Sixty-seventh Annual Meeting of the Louisiana State Medical Society, New Orleans, May 14, 1947.

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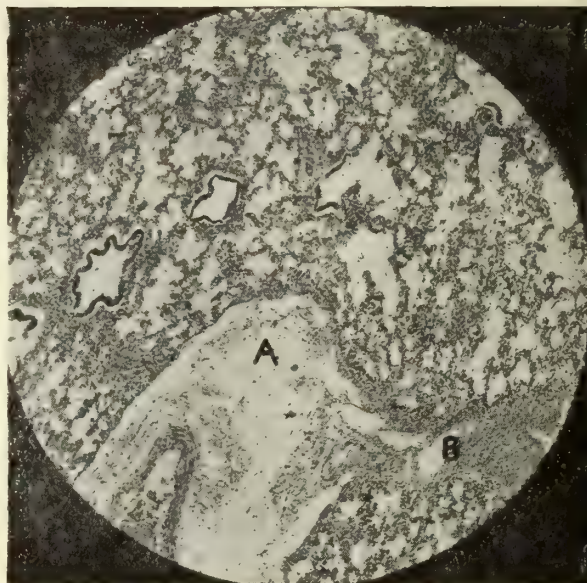
is the primary pathology. Experimental evidence<sup>2</sup> indicates that the site of escape is through the bases of alveoli which lie upon the smaller blood vessels. This escape is likely to take place (a) when alveoli are overinflated without corresponding increase in the circumference of the underlying vessels, or (b) when the circumference of the vessels is decreased without reduction in the size of the alveoli. Increased alveolar pressure in either instance increases the likelihood of escape of air. The caliber of the blood vessels may be reduced in several types of congenital heart disease or by forced expiration leading to reduced return of blood to the right heart and correspondingly to the pulmonary circulation.

Clinical conditions which may lead to the production of pulmonary interstitial emphysema are not uncommon in the early newborn period. These include atelectasis of a degree to be pathological; any type of congenital heart disease which decreases the volume of pulmonary blood flow; the irregular respiration sometimes caused by intracranial hemorrhage; excessively vigorous methods of resuscitation; and aspiration of meconium, mucus, or excessive amounts of amniotic fluid. Normally, the expansion of airless lungs, necessary to establish respiration, requires a much greater negative pressure than does normal respiration, probably because of cohesion of the moist surfaces of the air passages in the collapsed state.<sup>7</sup> Moreover, extensive changes in both the cells lining the alveoli and the connective tissue of the lung occur with expansion of the lungs. When all of these factors are considered it becomes apparent that the ability of the respiratory passageways to act as an airtight container receives a severe test in the newborn period.

#### PATHOLOGY

I have examined a small series of newborn infants coming to necropsy for various reasons and found pulmonary interstitial emphysema to be quite common.<sup>8</sup> It is difficult to draw any conclusion, however, because so many of the infants have had artificial respiration which may lead to a false high incidence. Nevertheless, I believe pul-

monary interstitial emphysema to be quite frequent in amounts insufficient to cause significant harm. Less frequently it is present in larger amounts and may cause hemorrhage in the lung; splint the lung in a state of inflation, thus limiting the respiratory excursion; and by its perivascular location lead to a partial block in the pulmonary circulation. Some of these changes are seen in figures 1 and 2.

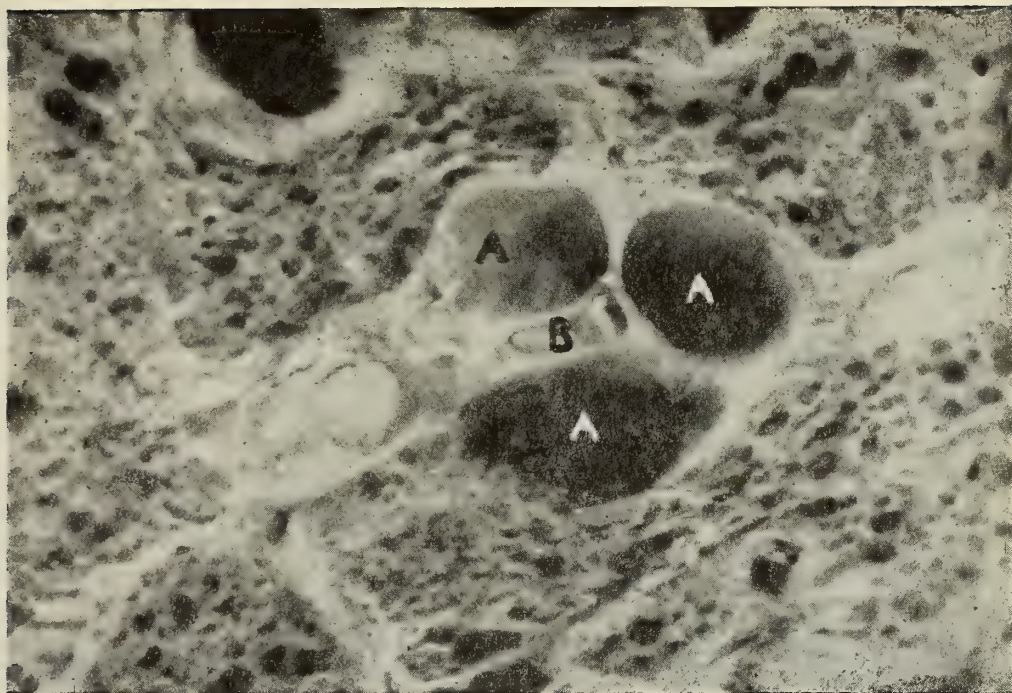


#### LEGEND:

Fig. 1: Photomicrograph (approximately x116) of a section from the lung of a newborn infant dying of airblock. At A is a large perivascular collection of air. Note the hemorrhage which extends beyond B along a connective tissue plane.

There is excellent clinical evidence that in newborn infants interstitial emphysema may rupture the visceral pleura directly to produce pneumothorax: of six infants with airblock coming to autopsy, pulmonary interstitial emphysema and pneumothorax were present in all, yet mediastinal emphysema was present in only one.<sup>4</sup> In three of these six patients the pulmonary interstitial emphysema was particularly marked near the hilus of one or both lungs, suggesting that this may be the site of rupture of the visceral pleura. When pneumothorax is produced it frequently develops a pressure higher than atmospheric, probably because





## LEGEND:

Fig. 2: Very low power magnification (approximately  $\times 15$ ) of the cut surface of the fixed lung of a newborn infant dying of airblock. At A are large collections of air surrounding a blood vessel, B. Note the generalized ectasia. Some of these collections of air are in normal passageways, but many are in the interstitial tissue.

of strong expiratory effort “pumping” air into the pleural space.

Interstitial air in the lung may not rupture the visceral pleura but may travel along the great vessels to the mediastinum to produce mediastinal emphysema.<sup>6</sup> If a pneumothorax has already been produced by rupture of the visceral pleura and the site of this rupture is near the lung root (as above suggested), there is no reason why mediastinal emphysema may not also be produced: as the pressure in the pleural cavity rose there would be an increased likelihood of air continuing into the mediastinum. From the mediastinum the air may rupture the mediastinal pleura to produce pneumothorax;<sup>9</sup> theoretically, the pneumothorax could be either on the same or the opposite side, or even on both sides. The deleterious effect of mediastinal emphysema in newborn infants has been widely described. However, it is not always easy

to determine what portion of the harm is due to the mediastinal emphysema and what to the pulmonary interstitial emphysema. Nevertheless, it can be said that in the newborn infant with mediastinal emphysema, and no doubt pulmonary interstitial emphysema, aspiration of the former will relieve alarming symptoms.<sup>9</sup> In animals, where mediastinal emphysema without pulmonary interstitial emphysema can be produced experimentally, the harmful effects of the former are probably due to pressure of the air on the great vessels, particularly the large veins.<sup>10</sup>

From the mediastinum the air can travel upward into the cervical subcutaneous tissues or downward along the great vessels into the retroperitoneal tissues to produce pneumoperitoneum. Extension of the air to extrathoracic locations is not a serious complication and may actually be accompanied by clinical improvement, the pressure

inside the chest having been diminished.<sup>1</sup>

There are two aspects of the subject which need further investigation. The first is the effect of pulmonary interstitial emphysema upon the heart. When extensive, because of its perivascular location, pressure on the vessels, and consequent block to the pulmonary circulation, it must lead to cor pulmonale. The second is the probability of air embolism.

#### SYMPTOMATOLOGY

There is no report, to my knowledge, of an autopsy on a newborn infant in which the sole finding which could have caused the death was pulmonary interstitial emphysema. For this reason an authoritative correlation of pulmonary interstitial emphysema with a definite clinical picture cannot be made. I suspect, however, that many of the symptoms and signs mentioned below, which have been seen in infants having pulmonary interstitial emphysema with mediastinal emphysema and infants having pulmonary interstitial emphysema with pneumothorax, can be caused by pulmonary interstitial emphysema alone. These symptoms are, of course, seen in only the more severe cases; as already mentioned, small amounts of aberrant air probably cause little harm and produce no symptoms.

The outstanding symptoms of mediastinal emphysema with pulmonary interstitial emphysema are dyspnea and cyanosis. In the more severe instances the chest becomes expanded and in spite of marked effort the infant is able to no more than partly expire. Consequently the respiratory excursion is greatly reduced, although the respiratory rate may be considerably increased. The neck veins may become visibly distended. The area of mediastinal and cardiac dullness may be diminished. The heart sounds may be faint and distant; the crackling crunching sound synchronous with the heart beat that has been often described in adults is less frequently heard in newborn infants. Although adults may complain of pain, this symptom is difficult to evaluate in the newborn period. If palpable cervical subcutaneous emphysema appears, the diagnosis is greatly reinforced.

The symptoms of pneumothorax with pulmonary interstitial emphysema are similar in many respects to those of mediastinal emphysema with pulmonary interstitial emphysema. Dyspnea and cyanosis are common to both. Similarly, in the more severe instances the infant may have an expanded chest and expiration be difficult and limited. The neck veins may be distended. The cardiac findings, however, are different. Instead of distant heart sounds and the crunching sound, the heart is likely to be shifted either to the right or to the left. Over the pneumothorax the characteristic changes in percussion and auscultation may be obtained. Cervical subcutaneous emphysema does not occur.

If pulmonary interstitial emphysema, mediastinal emphysema, and pneumothorax—all three—are present, all of the symptoms and signs mentioned in the two preceding paragraphs may be present.

#### X-RAY FINDINGS

Although a roentgenographic diagnosis of pulmonary emphysema may offer little problem, the differentiation of compensatory from obstructive emphysema may be more difficult. Inspiratory and expiratory films are required;<sup>11</sup> in infants these are difficult to obtain accurately. Moreover, once a diagnosis of obstructive emphysema is made, it may be impossible to decide whether the major portion of the air is on the inside or outside of the normal passages. If escape of air from the normal pathways is as frequent as my experience indicates, both compensatory and obstructive emphysema, more particularly the latter, are frequently complicated by interstitial emphysema. For this reason any marked emphysema of recent acute onset may lead to suspicion of interstitial emphysema.

A roentgenographic diagnosis of mediastinal emphysema is not always easy. An anteroposterior or postero-anterior film of the chest may show a curvilinear shadow of air along either margin of the mediastinum or along the border of the heart. A lateral view may show a large collection of air in the anterior mediastinum. However,



neither of these views is absolutely reliable; extensive mediastinal emphysema may be present yet these views fail to show it. If a pneumothorax is also present the value of the lateral view is further reduced: air in the pleural cavity, particularly if under tension, can produce on the lateral film a shadow identical with that produced by air in the anterior mediastinum.<sup>4</sup> Moreover, it is likely that severe emphysema in the anterior portion of the lung may also cause an apparent substernal collection of air. This would be particularly true if the film were slightly overexposed.

The roentgenographic characteristics of pneumothorax are well known. It should be emphasized, however, that there may be no relation between the size of a pneumothorax and its pressure. A comparatively

small pneumothorax may be under very high tension as evidenced by increased distance between the ribs, depression of the diaphragm and shift of the mediastinum. If the underlying lung contains sufficient interstitial air, it splints the lung in an expanded position and, being trapped there, prevents more than moderate collapse. Similarly, if the opposite lung is involved, it may be so expanded as to prevent shift of the mediastinum, although the pneumothorax of the opposite side is under very high tension as evidenced by widely spaced ribs and depressed diaphragm.

Some of the x-ray changes mentioned above are illustrated in figure 3.

#### TREATMENT

A review of the known etiologic factors suggests that measures designed to avoid



#### LEGEND:

Fig. 3: X-rays of the chest of a newborn infant with airblock who died a few hours later. Reproduced from the *Journal of Pediatrics* (4) by permission of the editors. A: Anteroposterior view. There is atelectasis of the right upper lobe. The left pneumothorax is evidently under great tension. Note the widely spaced ribs, shift of the mediastinum, and depression of the left diaphragm. Yet the left lung is only partially collapsed. Further collapse is prevented by pulmonary interstitial emphysema, air trapped in the tissue of the lung.

B: Lateral view. The apparent substernal collection of air is not due to mediastinal emphysema; there was no air in the mediastinum at autopsy. The shadow is due to herniation of the anterior mediastinum by the tension left pneumothorax.

the occurrence of airblock must be largely a matter of the best obstetric attention possible, together with careful resuscitation of those infants needing such measures. If extensive atelectasis suggests the advisa-

bility of bronchoscopic aspiration, this procedure is feasible in the newborn period.<sup>12</sup>

It is likely that in most instances the amount of aberrant air is small, causes few or no symptoms, and needs no treatment. In many more the amount of aberrant air is so small as to produce only mild symptoms; in such cases the only indicated treatment is the administration of oxygen and gentle care of the infant.

In more severe cases some effort to remove portions of the aberrant air may be advisable. If a large or tension pneumothorax occurs, aspiration may be indicated; this may have to be repeated several times. Gumbiner and Cutler<sup>9</sup> have reported the alleviation of alarming symptoms following aspiration of the anterior mediastinum in a newborn infant with mediastinal emphysema. An effective therapeutic approach to pulmonary interstitial emphysema has not been devised.

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## POSTMORTEM OBSERVATIONS IN TWENTY-TWO PREMATURE INFANTS\*

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This paper is not intended to be a statistical survey of the causes of death of premature infants dying during the neonatal period. Adequate reviews of this subject, based on autopsy findings, have been presented in the papers by Potter and Adair,<sup>1</sup> Potter,<sup>2</sup> Cruickshank,<sup>3</sup> D'Esopo and Marchetti<sup>4</sup> and Macgregor.<sup>5</sup>

Although pathologic findings, presumably indicative of the cause of death can be demonstrated in 70 to 88 per cent of viable premature infants dying in the neonatal period, many clinicians and pathologists still feel that autopsies on premature infants are of little value, as they consider prematurity alone to be an adequate cause of death. The responsibility for this misconception rests both with the clinician and the pathologist. The clinician has been lax in obtaining permissions for post mortem examinations on premature infants dying in the neonatal period, and the examinations performed by the pathologist on such infants are usually inadequate. The present paper is presented to encourage better cooperation between the clinician and the pathologist in dealing with premature infants. This cooperation is badly needed, for there is probably no period of life during which clinical diagnoses are so unreliable.

The material for the present paper consists of the consecutive autopsy records of 22 premature infants dying during the neonatal period on the Tulane Service of the Charity Hospital of Louisiana at New Orleans. The deaths occurred between October, 1945 and May, 1946. All the infants were born alive, weighed more than 499

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grams and less than 2500 grams, and died between five minutes and 25 days after birth. Twenty were colored and two were white. Complete postmortem examinations including examination of the contents of the cranial cavity were carried out on all infants. Bacteriologic studies were inadequate since most of the bodies were unclaimed and the autopsy, by law, could not be done until 48 hours after death. All the autopsies were performed by the author.

Among the 22 premature infants five were classed as previable (weight 500-999 grams). An adequate cause of death was demonstrated in four of these. There were 17 classed as viable premature infants (weight 1000 to 2499 grams). An adequate cause of death was demonstrated in all of these infants (Table 1).

In the entire group of 22 infants 16 died in the first 24 hours after birth, two died between 24 and 48 hours and four died between 14 and 25 days (Table 1). All of the previable premature infants died within 48 hours and only one lived over 24 hours.

The causes of death in the previable premature infants were bronchopneumonia, two, and intracranial hemorrhage, two. No cause of death could be demonstrated in one infant weighing 904 grams and living one hour and 36 minutes. The causes of death in the viable premature infants were congenital syphilis, five, bronchopneumonia, four, asphyxia, four, thrombosis of the venous sinuses of the dura mater, two, and intracranial hemorrhage, two.

In the entire group of 22 infants bronchopneumonia was the immediate cause of death in six, congenital syphilis in five, asphyxia in four, intracranial hemorrhage in four, dural sinus thrombosis in two and the cause of death could not be determined in one. Infection, including congenital syphilis, was held accountable for 11 of the 22 deaths (Table 1).

In the 16 infants dying during the first 24 hours there were four cases each of bronchopneumonia, congenital syphilis, and asphyxia, three of intracranial hemorrhage and one in which the cause of death could not be determined. Only two infants died

between 24 and 48 hours, one of an intraventricular hemorrhage and one of congenital syphilis. There were two infants with bronchopneumonia and two with dural sinus thrombosis who died between 14 and 25 days (Table 1).

These figures are too small to be of any statistical significance but they do show that even in premature infants important pathologic changes can be demonstrated by careful postmortem examinations. The detailed findings should be of interest to obstetricians and pediatricians.

Bronchopneumonia was present in six cases as the immediate cause of death and occurred in infants dying from 17 minutes to 25 days after birth. It was present as an incidental factor in four others, three dying of congenital syphilis and one of lateral sinus thrombosis. The intensity of the process varied considerably, being more severe in the infants who lived over 48 hours. In these cases it probably represented a postnatal infection. Three of the four infants dying during the first 24 hours of bronchopneumonia showed microscopic evidence of aspiration of amniotic sac contents. In two infants the inflammatory reaction was slight and asphyxia may well have been more important than pneumonia as the immediate cause of death. Macgregor<sup>6</sup> believes that some cases of pneumonia with prenatal aspiration may be caused by a non-bacterial irritant in the aspirated material. In 541 consecutive autopsies on infants up to 28 days old, she found inflammatory changes in the lungs in 37 per cent of the live-born infants and in 11.8 per cent of the dead-born. Premature infants appeared to be especially susceptible to respiratory tract infections. Johnson and Meyer<sup>7</sup> believe that a clinical diagnosis of congenital pneumonia is practically impossible, and that nearly all infants dying of pneumonia within three days after birth do so as a result of antenatal infection.

Congenital syphilis accounted for five deaths in the present series. All of these occurred in viable premature infants dying between one hour and 30 minutes and 34

hours after birth. Congenital syphilis may manifest itself only by osseous changes (Schmidt,<sup>8</sup> Schneider<sup>9</sup>) but in the present series, although bony changes were constant, other evidences of congenital syphilis were also present. These included hepatomegaly and splenomegaly, syphilitic pancreatitis and in one infant extensive fibrosis of the hypophysis. A similar change in the hypophysis has been described by Browne<sup>10</sup> who found syphilis to be the most important form of antenatal infection. Potter,<sup>1</sup> however, found congenital syphilis in only two of 954 autopsies on infants dying during the intrauterine and neonatal periods. Cruickshank<sup>11</sup> has pointed out that syphilis in the mother is not an important cause of abortion but is an important cause of premature delivery. The appalling incidence of congenital syphilis in the present series, in spite of the small number of cases, demonstrates the continued importance of syphilis as a public health problem, at least among the Negro race in the New Orleans area.

Asphyxia accounted for four of the deaths. All were viable premature infants dying in the first 24 hours. There is still disagreement as to the occurrence of intrauterine respirations in the normal human fetus. Small amounts of amniotic sac contents are often found in the lungs but it is generally agreed that a large amount is indicative of fetal asphyxia. Amniotic sac contents in the lungs may be identified by the presence of cornified epithelial cells and also by a pink staining coagulum applied to respiratory surfaces—the so-called asphyxial membrane (Johnson and Meyer<sup>7</sup> “hyaline membrane”; Farber and Sweet<sup>12</sup> “vernix membrane” and Baar<sup>13</sup>). Cornified epithelial cells derived from the skin of the fetus may be entrapped in this membrane or may lie free in the bronchioles and alveoli. In the lungs of the four infants in the present series whose deaths were attributed to asphyxia there were keratinized epithelial cells in the air spaces and a pink amorphous membrane lining many of the bronchioles and alveoli. Wilson and Farber<sup>14</sup> believe that actual bronchial obstruction due to as-

piration of the contents of the amniotic sac is less frequent in premature than in full term infants, as the production of vernix and cornification of the skin take place largely in the last months of pregnancy.

In addition to the four infants in whom death was attributed directly to asphyxia, eight others showed evidence of aspiration of amniotic sac contents varying from slight to moderate. In these cases asphyxia may have been a contributory cause of death. Two infants showed a few small foci of subependymal encephalomalacia in the white matter neighboring the lateral ventricles. Such lesions may be the result of asphyxia or of birth injury, but in themselves did not appear to be important factors in causing death. These focal subependymal necroses have been carefully described by Schwarz,<sup>15</sup> and Benda<sup>16</sup> has reported similar lesions in the brains of mentally deficient children.

Intracranial hemorrhage was responsible for four of the deaths. One infant showed an extensive subarachnoid hemorrhage and scattered petechiae in the substance of the brain; two showed subarachnoid, intraventricular and small intracerebral hemorrhages and one showed an intraventricular hemorrhage and petechiae in the brain. Two of the four cases occurred in previable premature infants. The duration of life varied from five minutes to 31 hours. In no instance was there an associated tear in the falx or tentorium. There is a difference of opinion as to whether intracranial hemorrhages without gross dural tears are the result of birth trauma or of asphyxia, and Holland<sup>17</sup> has pointed out the difficulty in distinguishing between traumatic and asphyxial intracranial hemorrhage.

Thrombosis of the dural sinuses was responsible for two deaths. Both occurred in viable premature infants living 14 and 18 days. No local inflammatory basis for the thrombi could be demonstrated. In one infant both lateral sinuses were thrombosed and in this case there was an associated bronchopneumonia. In the other infant there were thrombi in the superior sagittal



and lateral sinuses and in the great vein of Galen. This infant also showed subarachnoid, intracerebral and intraventricular hemorrhages. Bailey and Hass<sup>18, 19</sup> and Byers and Hass<sup>20</sup> have emphasized the importance of acute nutritional disturbances

together accounted for 11 of the deaths. Other causes of death were asphyxia, intracranial hemorrhage and dural sinus thrombosis. These findings indicate that prematurity uncomplicated by other disorders is seldom the sole cause of death.

Table 1  
Status of Prematurity

Cause of Death	Previaible Duration of Life			Viable Duration of Life			Total No.
	1-24 hrs.	25-48 hrs.	14-25 days	1-24 hrs.	25-48 hrs.	14-25 days	
Bronchopneumonia	2			2		2	6
Intracranial hemorrhage	1	1		2			4
Congenital syphilis				4	1		5
Asphyxia				4			4
Sinus thrombosis						2	2
Undetermined	1						1
	<hr/> 4	<hr/> 1	<hr/> 0	<hr/> 12	<hr/> 1	<hr/> 4	<hr/>
Total by length of life status	4	1	0	12	1	4	
Total by status		5			17		22

in the pathogenesis of dural sinus thrombosis in early life.

#### DISCUSSION

It cannot be denied that prematurity was an important contributing factor in the death of many of these infants. Prematurity, for example, favors the occurrence of such lesions as intraventricular hemorrhage.<sup>5</sup> It is also true that the full term infant may survive trauma and infections which might kill the premature infant. Thus obstruction of scattered bronchioles and alveoli may have little effect in the full term infant, owing to the relatively large pulmonary reserve. In the premature infant the total functional pulmonary parenchyma may be barely sufficient to maintain life and minor obstruction in the respiratory tract can be fatal.

The purpose of this paper is not to belittle the importance of prematurity as a factor in neonatal deaths but rather to show that if death occurs serious lesions can be demonstrated as the immediate cause in most instances. It is encouraging that many of the deaths were not the inevitable consequence of prematurity but were theoretically preventable.

#### SUMMARY

An adequate cause of death was demonstrated at autopsy in 21 of 22 premature infants dying during the neonatal period. Bronchopneumonia and congenital syphilis

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## THE PRESENT STATUS OF THE POLIOMYELITIS PROBLEM\*

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It is quite appropriate that poliomyelitis should be a topic for discussion at a meeting of the Louisiana State Medical Society because it was a physician in this state who reported the first epidemic of the disease in this country. The author of this brief report, George Colmer, practiced in the Florida Parishes and resided, at the time of his report, 1841, in Springfield, Livingston Parish.<sup>1, 2</sup>

My report, although somewhat longer, lacks the originality of Colmer's because it is not based on original investigation but rather on a review of recent literature made for the purpose of finding out where we stand in this problem. As time does not permit a complete discussion of so broad a subject, my remarks may be colored by my own interpretation and I shall be forced to disregard a careful balance of both sides of some controversial topics.

In talking with a group of practicing physicians who have varied and broad interests and are primarily concerned with the more practical aspects of medicine, one is always tempted to emphasize diagnostic and therapeutic procedures. Despite the fact that our knowledge of the disease is increasing rapidly and that investigation will lead eventually to more specific methods of diagnosis and treatment of the acute infection,

I should warn you at the beginning that I have little to offer in that regard.

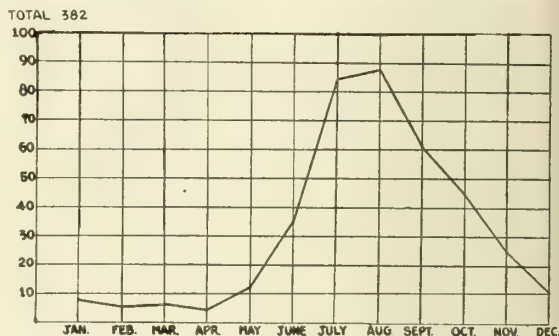
### ORGANISM

The virus of poliomyelitis is one of the smallest known and, as is true of filtrable viruses in general, propagates only in living cells. It is, however, resistant to freezing, drying and many protoplasmic poisons and may be preserved in the ice chest, in nervous tissue, for several years. It is neurotropic, in fact "neuronotropic", in that it combines preferentially with the neuron itself rather than the glial elements of the nervous tissues.

### EPIDEMIOLOGY

The seasonal incidence of the disease, with prevalence in the summer months, is well known. If it occurred only during that period of the year, study of the epidemiology might be much more simple, but the fact remains that it occurs in endemic form throughout the year. Cases are seen, even in the Northern states, during the winter months. The distribution of reported cases during the 1946 epidemic in Louisiana is shown in figure 1.

CASES OF POLIOMYELITIS IN LOUISIANA - 1946



### LEGEND:

Fig. 1: Monthly incidence of poliomyelitis in Louisiana during 1946.

The mode of transmission has been studied intensively in recent years and many facts, which may lead to methods of prevention, are known. Presence of the virus in the pharyngeal mucus as well as the pharyngeal tissues of persons ill with the disease has quite naturally led to the belief that droplet dispersion may play a role in transmission. It is also known that the virus

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is usually demonstrable in the intestinal walls and feces of infected persons as well as healthy contacts.<sup>3</sup> Trask, Paul and others<sup>4, 5</sup> have demonstrated the virus in urban sewage during epidemic periods. It has not been found in water supplies. It has also been detected in the bodies of various species of flies trapped in epidemic areas.<sup>6, 7, 8</sup>

The bulk of evidence now favors fecal contamination as an important method of transmission. With the seasonal incidence of the disease parallel to that of the fly population, one is tempted to conclude that flies may play the same role in mechanical transmission of the virus that they do in typhoid fever or dysentery. More information must be gathered, however, before precise interpretations can be made. For instance, it will be necessary to know the survival times of the virus outside of the body in feces, mucus and food and the minimal infective dose for man.

#### PATHWAYS OF INVASION

It has been quite definitely established that having gained entrance to the animal body, the virus is transmitted along healthy nerve fibers. This has been demonstrated repeatedly by the following rather simple experiment. If a sciatic nerve is sectioned and the virus suspension applied to the proximal cut end, poliomyelitis invariably results after an incubation period of four to six days. If, on the other hand, the nerve is cut or even frozen, proximal to the point of application of the virus, no infection results.

In the macacus rhesus monkey, which was practically the only animal used for this work prior to 1938, the disease can be produced readily by application of the virus to the nasopharynx but not to other mucous membranes or the skin. If the olfactory nerves of this animal are sectioned, invasion does not take place no matter where the virus is applied externally. Thus, as long as our observations were confined to the macacus rhesus, the problem was simple. The portal of entry was the nasopharynx.

It has become increasingly evident that conclusions regarding the portal of entry in man cannot be based on observations in

the rhesus monkey for many reasons, foremost among which is the fact that the virus is not usually found in the stools of infected animals of that species and that entry via the gastrointestinal tract may be barred by intestinal secretions or some other mechanism.

There are many reasons to believe that the portals of entry in the chimpanzee may be more similar to those in man. As is also true in man, the virus can be recovered from the stools, and two young chimpanzees in a zoo are reported to have contracted the disease spontaneously during an epidemic.<sup>9</sup>

In one series of experiments by Howe and Bodian,<sup>10</sup> six chimpanzees were inoculated in pairs with human stools containing poliomyelitis virus. Two animals received the inoculum intranasally, two intraorally and two by stomach tube. In each of the last two pairs, one animal had been subjected to bilateral olfactory tract section. All of the animals contracted poliomyelitis. The entire brain stem and considerable portions of the cortex, spinal cord and peripheral nervous system were studied by serial section. Lesions of the olfactory bulbs and secondary olfactory nuclei were present only in the animals receiving intranasal inoculations. There was good correlation between the development of bulbar paralysis and intraoral inoculation. In the animals receiving stomach tube inoculations, there was histologic evidence that the virus had reached the brain from the spinal cord. Another animal, not included in this series, was killed before paralysis and showed lesions of the coeliac and sympathetic chain ganglia but none of the central nervous system.

Studies on the portal of entry in man must be approached more indirectly and are therefore less conclusive than in other animals. Two methods have been used: pathologic analysis of the distribution of lesions and virus assay of tissues. Neither of these methods is entirely satisfactory because at the time of death, the virus is widely disseminated. Furthermore, histologic methods of tracing the spread of infection are available only for nervous tissues. His-

tologic findings show that the olfactory bulbs are capable of reacting to the virus but indicate that the olfactory portal is not involved in most cases.

Many facts point to the alimentary tract as a focus of virus proliferation and the spinal cord as the primary site of invasion of the central nervous system in man. Critical evidence of the abdominal sympathetic system as a route to the spinal cord has not been produced but it can be strongly suspected on the basis of the demonstration of both the virus and histological lesions in the coeliac ganglion of chimpanzee and man.

#### SYMPTOMATOLOGY AND PATHOLOGY

As this group of practicing physicians is no doubt familiar with the symptoms of the disease, I shall not take the time necessary to recite them from the textbook but shall attempt rather to review the course of the disease in relation to our knowledge of the underlying pathology and immunology.

We have reviewed the mode of transmission and the evidence available regarding invasion of the nervous system. The virus having entered the nervous system, one of three courses may follow: The disease may be arrested in the "abortive" or "non-paralytic" stage, paralysis with recovery may take place or permanent paralysis may result.

The first symptoms of the disease are fever, headache, pharyngitis, vomiting and diarrhea. These are followed in one to three days by irritability or drowsiness, muscle tenderness, stiffness of the neck, rigidity of the spine and positive Kernig sign. These symptoms usually appear seven to 14 days after exposure. Examination of the spinal fluid at that time usually reveals 50-100 cells, although the count may be higher or lower. Polymorphonuclear leucocytes may be present during the first few days but lymphocytes predominate. The globulin content of the spinal fluid is normal or slightly increased at first but gradually increases. From the clinical standpoint, the disease may not, and probably in the majority of cases does not, progress beyond that stage. The existence of non-paralytic cases in man is, of course, difficult to estab-

lish. In the experimental animal, however, it can be confirmed histologically and by virus assay.

When virus reaches the central nervous system, one of several sequels is possible. If the dose is subinfective for the cells near the site of entry, the virus may be sterilized there. If the dose is somewhat larger or the tissues more susceptible, a local pathological response to invasion and injury at the site of entry may occur, followed by sterilization before the virus can multiply and spread to other susceptible centers, or there is multiplication and spread to other susceptible centers.<sup>11</sup> Failure of multiplication and spread and injury to a comparatively few cells probably accounts for the majority of non-paralytic cases. The absence of demonstrable paralysis in many cases is probably due to the fact that the distribution of destroyed motor neurons is too scattered to involve a single functional muscle group sufficiently to produce clinically evident loss of function. In such cases, one may find all the anterior horn cells destroyed in one microscopic section and another section a millimeter away unaffected.

It is generally agreed that a large portion of cases never progress beyond the non-paralytic stage. The extent of invasion beyond this point is dependent upon the balance between virulence of the organism and susceptibility of the host. When paralysis occurs, weakness is usually observed and reflexes diminished by the third day after onset of symptoms. The maximum degree of paralysis is reached in a few hours to two or three days and the fever usually falls by lysis in four or five days.

Of those in whom a definite weakness can be demonstrated, approximately 25 per cent show complete clinical recovery, five to ten per cent die, and the remainder have some degree of residual paralysis.

Time does not permit a careful discussion of the morphologic changes which take place in the nervous system as the disease advances. Briefly, the major lesions consist of degeneration of the anterior horn cells of the spinal cord and motor nuclei of



the cranial nerves and, in the acute state, widespread inflammation throughout the nervous system. The virus migrates along the living axon and is distributed widely throughout the central nervous system. How it can pass through certain neurons without producing injury remains a mystery but it seems likely that chemical differences exist and that the type of cell-selectivity found in other virus diseases may apply.

#### PREVENTION

The possibilities of establishing effective control of the disease fall into three categories: prevention from exposure, passive immunization and active immunization.

Our knowledge of the transmission of the disease is so limited that few definite recommendations can be made on the control of exposure but I would warn against questionable measures which encourage public panic.

On the basis of evidence that the virus may be recovered from the pharynx, protection of children from exposure to infected persons and from crowds during epidemics may be justified but it seems unlikely that droplet dissemination will prove to be the primary method of transmission. Control of spread of the virus from one intestinal tract to another may be a more efficient approach. As in typhoid, healthy carriers have been recognized and patients who have recovered from either the paralytic or non-paralytic types of disease carry the virus in their intestinal tracts for various periods. It presents a much more difficult problem than typhoid, however, because the virus can be identified only by animal assay and that is too expensive and time-consuming a procedure to be carried out on a large scale. Our current methods and duration of isolation are arbitrary and not based on scientific evidence.

Attempts to control exposure by nasal sprays have not proved efficacious. They were based on the assumption that the primary portal of entry in man, as in the rhesus monkey, is through the olfactory tract and that assumption is no longer valid.

Considerable attention has been given recently to the problem of tonsillectomy in

relation to poliomyelitis. Children who develop the disease shortly after tonsillectomy are more likely to have it in the fatal bulbar form and the incidence may be higher among this group. Until better evidence that it is a safe procedure is available, it would seem advisable to avoid tonsillectomy during epidemics. This does not mean that the operation should not be performed during the summer months in years or areas in which the prevalence of the disease is not increased.

On general principles, it does not seem likely that passive immunization offers much hope as a preventive measure. The best we can hope for is that a concentration of antibodies, such as is found in human gamma globulin, may offer temporary protection to children known to have been exposed, if given before the virus enters the body. The evidence at present is discouraging.

Active immunization is a topic of much more lively interest. It offers the most hopeful approach to the control problem that we know at the moment but the ideal vaccine has not yet been discovered. The disappointing results which followed the use of killed and chemically attenuated viruses are well known. When the killed virus was used, apparently no protection resulted. When the chemically attenuated virus was used, it was not sufficiently attenuated and children developed the disease. Much work has been done recently on mouse-adapted strains and on attenuation of the virus by irradiation and other physical means. One of the limitations in all of this work is the fact that the presence of neutralizing antibodies in the circulating blood may not guarantee protection of the neuron. Neutralizing antibodies have been demonstrated very early in the disease. This suggests that they were present at the time of exposure and did not serve a protective function. Furthermore, second attacks have been reported, although it is quite possible that both attacks were not caused by the same strain of virus.

#### THERAPY

Regarding specific therapy in the acute phase of the disease, there are few encour-

aging leads. Numerous drugs, including the sulfonamides and penicillin, have been tried and have failed. Fifteen years ago it was thought that convalescent human serum was the answer but most investigators now agree that it is of no value.

Use of the concentrated gamma globulin fraction of pooled adult human serum in preparalytic poliomyelitis has been the subject of considerable active research recently. Neutralizing antibodies against the Lansing strain of poliomyelitis are said to be present in this fraction at an average concentration 18 to 25 times as high as that in the corresponding whole plasma. Bahlke and Perkins<sup>12</sup> conducted a very critical investigation of the efficacy of gamma globulin during the 1944 epidemic in New York State. Their conclusions are, "In a series of 111 patients with preparalytic poliomyelitis observed for approximately six months after onset, no benefit is detectable when 56 of them who had received large doses of gamma globulin intramuscularly are compared with 55 alternate, untreated controls."

I shall not enter the controversy surrounding the orthopedic treatment of the disease once paralysis has developed. In general it appears that complete immobilization of extremities may be disadvantageous in many cases because it may lead to atrophy and increased loss of function. Application of heat relieves pain and when combined with active physical therapy, diminishes the extent of paralysis and deformity. Maintenance of centers where the disease can be treated actively in the early stages of paralysis is certainly justified.

The ramifications of this subject have made it necessary for me to review hastily a large amount of material. I have tried to indicate the directions in which progress may be expected. Despite the enormous amount of effort expended in the study of this disease in recent years, we are far from the goal.

#### DISCUSSION

Dr. Peters: What do you think about the CO<sub>2</sub> treatment?

Dr. Lippard: I have had no experience with it

and I do not understand the rationale underlying its use.

Dr. Levy (Baton Rouge): What has been your experience at Charity Hospital with those patients who have received sulfa drugs in the prodromal stage? Is it true that the paralysis has been worse?

Dr. Lippard: It is my impression from the literature that they have no effect on the disease one way or another. That would seem logical because the sulfa drugs are, in general, not antiviral in their action.

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## INTRAMEDULLARY INFUSIONS IN INFANTS\*

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AND

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NEW ORLEANS

More than 200 patients admitted to the pediatric wards of Charity Hospital in New Orleans have received fluids by intramedullary route since December, 1945. At that

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time a simplified procedure was established by the Tulane Pediatric Division; because no complications have occurred, our experiences and this technic deserve discussion.

In 1932 Drinker and associates<sup>1</sup> and Doan<sup>2</sup> independently suggested bone marrow as a route for administration of fluids. Tocantins and co-workers<sup>3, 4, 5</sup> enlarged on earlier work in this field, and published data regarding indications, rate of absorption, and complications. Since 1942 several reports from abroad have emphasized the usefulness of this route for fluid injections in properly selected patients. Heinild, Sondergaard and Tudvad<sup>6</sup> recently reported experiences with 1000 bone marrow infusions in six different Danish hospitals. They condemned long-continued infusions and intra-osseous injection of hypertonic or irritating fluids. They recommended the multiple syringe, "push" infusion as the most satisfactory method.

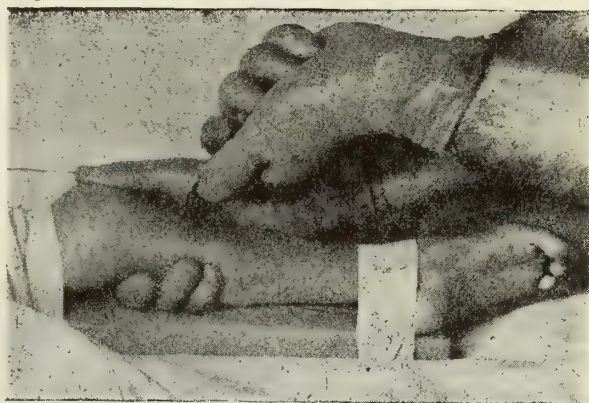
#### TECHNIC

Many methods of administering fluids into the medullary cavity have been described, some calling for elaborate needles or trephines, others requiring only minimal simple equipment. In our experience an 18 gauge, stainless steel needle with a well-fitting stylet is adequate; strength and a keen cutting edge are essential. For older infants a 16 or 17 gauge needle of the same quality may be employed.

The patient is prepared in the following manner: The lower extremity is fixed to a padded board so that the assistant operator's hand may support the knee. The upper two-thirds of the tibia is cleansed, then prepared with iodine or merthiolate followed by alcohol, as for any surgical procedure; sterile technic is used throughout. One c.c. of normal saline containing 10,000 units of penicillin is mixed with 0.25 c.c. of 1 per cent solution of procaine hydrochloride. A site is chosen in the mid-portion of the upper third of the medial (flat) tibial surface. Particular care is used to avoid proximity to the epiphyseal line. The penicillin-procaine solution is then infiltrated down to the periosteum.

A 5 c.c. Luer-lok syringe is attached to

the needle selected, and a small towel is wrapped around the syringe; this then serves as a handle. The needle is directed toward the knee not quite perpendicularly to the long axis of the tibia, and pressure is exerted while employing a slightly drilling motion. One hand supports the tibia



#### LEGEND:

Fig. 1: Puncture of tibial medullary cavity with 17 gauge needle with 5 c.c. Luer-lok syringe as handle. Note support of patient's extremity as pressure is applied.

during this maneuver (see fig. 1). Entry into the marrow cavity is easily appreciated by a sudden "give" or reduction in resistance. The bevel of the needle is directed cephalad, the syringe is removed, and a stylet introduced to be sure the lumen is



#### LEGEND:

Fig. 2: Introduction of stylet to insure patency of needle lumen. If bony core is present, a few thrusts will dislodge it.

clear (see fig. 2). The ease with which the bony cortex may be punctured is dependent upon skill of the operator, site chosen, age of

the patient, and perhaps certain deficiency syndromes. Despite these considerations, however, one often encounters extreme and unexplained variations in thickness, resistance, and brittleness of bone, and consequent minor technical difficulties which are easily overcome with experience. A few c.c. of saline is injected, and if this is blood-tinged when aspirated, the syringe is removed and the special infusion set is attached.

A year ago it was our policy to employ the multiple syringe method, so uniformly recommended throughout the literature. We now wish to introduce an infusion set, which, to the best of our knowledge, has not

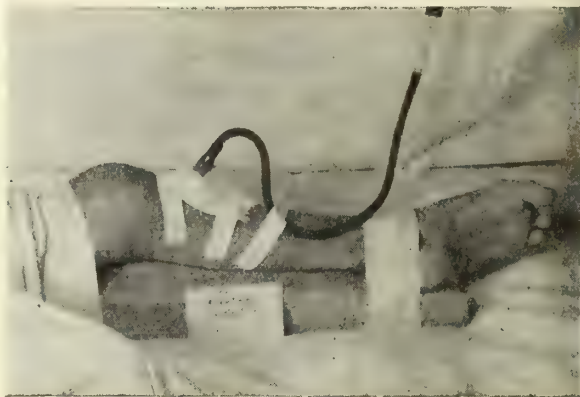
hitherto been described for this purpose (see fig. 3 and 4). This infusion set has many advantages. Once attached to the marrow needle, the system is closed. Because the valve is automatic and light in weight, the possibility of needle movement is minimized and likelihood of seepage into surrounding tissue reduced; the latter is a frequent complication of the multiple syringe method. Extreme simplicity of operation has increased its popularity. Almost any small syringe may be employed with this set, but for convenience, and to reduce potential pressure-pain, we ordinarily use a 5 c.c., 2 c.c., or even a tuberculin syringe for infants. Such a set is now standard equipment on our service, and will be described in detail elsewhere.

If a continuous infusion is desired, the marrow needle is fixed in place with flamed



LEGEND:

Fig. 3: Two-way automatic valve with small syringe attached ready for attachment to marrow needle. Note very thin plasma tubing.



LEGEND:

Fig. 5: Light weight BD Luer-lok adapter attached to marrow needle for marrow drip. Blood and plasma are difficult to administer by gravity alone, but less viscous fluids can be administered by this method.



LEGEND:

Fig. 4: Automatic valve attached to marrow needle. Mantoux syringe attached is popular because of extremely light weight and because only slight pressure is needed to force fluid.

adhesive and sterile gauze (see fig. 5). We have encountered no complications even when infusions have remained for as long as 72 hours, though usually they are not allowed to run for more than 12 to 24 hours. If additional parenteral fluids are required after this time, the preferred intravenous route is usually again available. Bone marrow infusions may be repeated, however, as often as necessary simply by varying sites of injection, but the same bone should



not be punctured again until at least 24 hours have passed.

Before the needle is removed, 10,000 units of penicillin in normal saline is injected partly into the medullary cavity and partly along the course of the withdrawing needle. We have done this routinely.

We do not recommend the intramedullary over the intravenous route, but use it rather as an alternative when veins are inaccessible. Just when patients most urgently need corrective fluid therapy, valuable time is often lost by attempting to enter collapsed or very small veins. Added trauma incident to such well-meaning efforts and the extra manipulations they entail, certainly appear further to depress an already debilitated patient.

#### REPORT OF A CASE

A recent illustrative incident occurred when a malnourished infant with a severe acute nutritional disturbance was admitted. Comatose, he exhibited all the classical features of marked dehydration and acidosis; the carbon dioxide combining power was 7 volumes per cent. There was twitching of the extremities and no discernible reaction to painful stimuli. Death appeared imminent. Fourteen venepunctures and two cutdown procedures had been attempted. Appropriate alkaline and fluid therapy was then administered by rapid, forced injection into the tibial marrow. Response was gratifying, and the infant was crying vigorously within an hour. Usual supportive and dietary measures were then employed, and a transfusion was given into the same needle six hours later. Uneventful recovery ensued.

We see many such emergencies among severely dehydrated infants brought to Charity Hospital, and it has been our policy to administer fluids immediately by the most expeditious route. Injudicious delay in administration of corrective solutions may be hazardous and may further accentuate existing water and electrolyte deficits. The rapid and almost foolproof technic for marrow infusions can be mastered by witnessing the procedure two or three times, whereas many intravenous technics useful for infants require time and skill and therefore often present insurmountable difficulties to the occasional or inexperienced operator.

We have successfully completed more than 200 intraosseous infusions in infants

and small children ranging from young prematures weighing as little as 964 grams (2 pounds, 2 ounces), and there have been no complications or sequelae. One patient received fourteen such infusions during a period of seven weeks. The puncture technic is not ordinarily used or recommended for children over the age of three, though there is no actual contraindication when an emergency exists beyond this age.

Pain, so obviously related to the pressure used for marrow infusions is ordinarily reduced or eliminated when the rate and pressure are reduced. Pain thus serves as a useful guide for controlling speed of fluid administration.

Tocantins and O'Neill<sup>4</sup> and Quilligan and Turkel<sup>7</sup> found frequent warnings in the literature two decades ago regarding local complications following prolonged administration of fluids into any single vein, and many incriminations of this now-common route also warn us of such dangers following cutdown procedures. Complications after intramedullary infusions into long bones; such as osteomyelitis, pressure occlusion of vessels, cellulitis, and subcutaneous abscesses, have been reported, though none of these are common. Quilligan and Turkel<sup>7</sup> found only 12 such among 1049 patients who had received fluids by intramedullary route. Five of these had mediastinitis, following sternal marrow punctures; five others had osteomyelitis of long bones.

We have not used the sternal route, and to reduce the possibility of infection, penicillin was infiltrated at the site of puncture before the needle was inserted, and again as it was withdrawn.

Queries have been received regarding rates of absorption for various types of fluids. While there is no doubt that fluids can be given more rapidly intravenously, rates attained in intramedullary infusions are ordinarily adequate. We give blood, plasma, or any of the physiologic repair solutions freely, employing usual dosage rules. Meyer and Perlmutter<sup>8</sup> found that the circulation time in human subjects measured from corresponding intravenous

and intramedullary sites was essentially similar in 21 subjects. They concluded that the intimate relationship between the general circulation and the medullary cavities warrants their use when venous channels are not readily accessible.

## SUMMARY

1. Intramedullary infusions should be reserved for patients whose veins are inaccessible.

2. The puncture principle, employing a short 16-18 gauge stainless steel needle is described.

3. Viscous fluids, such as blood and plasma, may not drip in easily by gravity alone; forced pressure injection is often necessary.

4. A two-way automatic valve with syringe pump seems more satisfactory than multiple syringe or continuous infusion methods.

5. All common infusion fluids may be administered by this technic at a satisfactory rate. Irritating solutions should not be used, lest tissue injury result.

6. We believe that absence of complications among these infants can best be attributed to careful technic, avoidance of the sternal route, use of penicillin at the site of marrow puncture, and to the closed system we ordinarily employ.

## DISCUSSION

Question (by student): Does seepage occur at the site? What bone other than the tibia do you use?

Dr. Sutton: We use the tibia in 95 per cent of the cases; in other cases the femur. The femur is good in permatuees.

Question (by student): Do you resterilize the needle and use it over again or use a new needle each time?

Dr. Sutton: I think the cost is so little that it justifies the use of a new needle.

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## HUMAN INFECTION WITH VIRUS OF EQUINE ENCEPHALOMYELITIS, EASTERN TYPE, IN LOUISIANA

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AND

MORRIS F. SHAFFER, D. Phil.†

NEW ORLEANS

Present knowledge of human infections with the virus of equine encephalomyelitis, Eastern type, rests largely upon studies performed on the 34 or more cases of the 1938 epidemic in Massachusetts, at least 24 of which were in children under ten years of age. Farber, Hill, Connerly, and Dingle<sup>1</sup> examined eight of these cases occurring in infants and children, reviewing the clinical features, diagnosis, treatment, pathologic and laboratory findings. Seven of the eight cases similarly reported by Wesselhoeft, Smith, and Branch<sup>2</sup> fell into roughly the same age group. The virus was isolated repeatedly at that time by Webster and Wright<sup>3</sup> as well as by Fothergill and associates,<sup>4</sup> but it does not appear to have been recovered from any subsequent instance of the disease in man. In 1941 Hammon<sup>5</sup> reported one case in an 8 year old girl, and in 1942 Bohls and Irons<sup>6</sup> recorded two probable infections in patients of unstated age. These three cases, occurring in Texas, were non-fatal; the diagnosis was based on clinical evidence supported by demonstration of specific virus-neutralizing properties in the patients' sera. To augment existing data, the following description of a recent fatal infection in a 6 year old girl from Louisiana is presented; isolation and identification of the virus are likewise reported.

## CASE REPORT

*Clinical History:* On the morning of August 3, 1946, B. H., a 6 year old white girl, resident of

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Houma, La., awoke complaining of headache. Her mother thought she had fever. She vomited twice during the afternoon. Following a short generalized convulsion she was taken to a local hospital where her temperature was found to be 101° F. No laboratory tests were performed, and after one injection of penicillin she was sent home. The patient played in her bed that evening, feeling better, but upon the reappearance of fever, headache, and vomiting next morning she was referred to the Charity Hospital of Louisiana at New Orleans.

Physical examination on admission disclosed a well-developed, well-nourished child who appeared moderately ill. She was stuporous but responded to stimuli and was cooperative when aroused. Kernig's and Brudzinski's signs were positive, hyperactive tendon reflexes were noted, and the pharynx was moderately injected. Temperature was 103.8° F., blood pressure 120/80 mm. Hg. Petechiae appeared on the abdomen within a few hours.

The initial hematologic examination showed 19,000 leukocytes per cu. mm. of which 88 per cent were polymorphonuclears, 12 per cent lymphocytes; the hematocrit was 34 per cent. During hospitalization two specimens of urine were examined and found normal; two blood cultures and a Mantoux test (0.1 mgm. O.T.) proved negative. The spinal fluid findings in four lumbar punctures are summarized in table 1 and are considered typical for viral encephalitis, though perhaps the initial content of leukocytes was higher than usual; smears and cultures from each specimen of fluid were reported as bacteriologically negative.

TABLE 1

SUMMARY OF FINDINGS ON EXAMINATIONS OF SPINAL FLUID FROM PATIENT B.H.

		Leukocytes						
Date		Pressure	Total	Per cent Pmn.	Pandy	Protein Mg./100 c.c.	Sugar Mg./100 c.c.	Chlorides Mg./100 c.c.
Aug. 4		250	1600	100	+	45	64	715
" 5		.....	760	90	+	55	60	585
" 6		460	510	82	+	93	84	644
" 6		.....	26 (?)	44	0	....	48	667

By 3:00 a. m. of August 5, recurrent convulsions and muscular twitchings had developed; the patient was unconscious, remaining so until death. After the first convulsion, plantar reflexes became extensor. Nystagmus and mild bilateral papilledema were noted. On August 6, the patient's condition deteriorated progressively. Mucus accumulated in the throat, and severe bilateral papilledema developed rapidly. The next day, August 7, she exhibited evidences of peripheral vascular collapse. Her temperature ranged between 104° and 106° F., blood pressure dropped to 85/60 mm. Hg.

At 5:00 p. m., bulbar symptoms increased, respirations became shallow, the face was flushed, and the patient died shortly thereafter.

Treatment was based on an initial presumptive diagnosis of pyogenic meningitis and included vigorous supportive measures. Sulfadiazine was given in dosage of 0.2-0.3 Gm./Kg. daily by hypodermoclysis. Ten thousand units of penicillin was administered intrathecally at the time of the initial spinal puncture; thereafter large amounts were given by intravenous, subcutaneous, and intrathecal routes. Repeated small transfusions of whole blood were given by continuous intravenous drip. Dehydration was controlled by parenteral administration of fluids to assure a total daily intake of 110 c.c./Kg. Concentrated plasma and 50 per cent glucose were given in an attempt to combat cerebral edema. Barbiturates were used for sedation. During the last two days of illness inhalations of 5 per cent carbon dioxide in oxygen were used in an effort to liquefy secretions. Adrenal cortical extract had no remarkable effect in altering the features of terminal collapse.

The final clinical diagnosis was viral encephalitis, type undetermined. Clinical and epidemiologic considerations justified suspicion of infection with the virus of equine encephalomyelitis.

*Postmortem Observations\**: Postmortem examination was restricted to the head. An extremely edematous brain weighing 1500 gm. was removed. No gross evidences of meningitis were found, but hyperemia and small hemorrhages were noted about the base. After removal of material for virus study, the remainder of the brain was fixed in formalin. Sections were later taken from the following regions and stained with hematoxylin-eosin: frontal, temporal and occipital lobes; wall of the anterior and posterior horns of the lateral ventricles; thalamus; mesencephalon; wall of the fourth ventricle; basal ganglia; cerebellum. Microscopic examination\*\* revealed similar changes in all samples of the brain. There were found in both the grey and white matter diffuse and focal areas of neutrophilic infiltration, the latter amounting sometimes to small abscesses. Accumulations of neutrophils and areas of demyelination were observed around many of the blood vessels; demyelination was noted especially at junctions of grey and white matter. The meninges exhibited small hemorrhages and moderate-to-severe infiltration of neutrophils, lymphocytes and macrophages.

*Virus Studies*: Several small portions of brain taken at autopsy shortly after death on August 7, 1946 were placed in glycerine and stored at 4° C.

\*We are indebted to Dr. E. S. Moss, Director, Department of Pathology, Charity Hospital, for permission to study specimens obtained at autopsy.

\*\*We are indebted to Dr. James B. Arey for examination of the sections.

On August 10, 1946 approximately one gram of this material was ground in a mortar and emulsified in broth. Groups of adult white mice were then inoculated by each of the following routes: intracerebral, intraperitoneal, intranasal, and subcutaneous. Six mice inoculated intracerebrally died within two to five days, and one mouse inoculated intraperitoneally died on the fifth day, each with signs characteristic of encephalitis in these animals.

The brains of the dead mice were emulsified and inoculated into other mice by the intracerebral route. This emulsion and similar preparations from later passages were found to be bacteriologically sterile; they contained an agent which passed through a Seitz EK filter disc and regularly killed white mice in 36 to 72 hours. In chick embryos, infection was lethal within 24 hours. The short incubation period in experimental animals suggested virus of equine encephalomyelitis; accordingly, an attempt was made to compare the agent isolated with known Eastern and Western types of equine encephalomyelitis virus† by means of cross-immunization and serum-protection tests.

Thirty-six mice were given a series of intraperitoneal injections of formalinized chick embryo vaccine prepared from the unknown virus. Groups were then challenged with varying dilutions of known strains of Eastern and Western types of equine virus. As shown in table 2, immunization with the agent under study protected mice against as many as 10,000 MLD's of Eastern type virus, but gave no significant protection against the Western type.

lactic effect. The results of one such experiment are summarized in table 3.

TABLE 3  
RESULTS OF PROTECTION TEST WITH EQUINE  
ENCEPHALOMYELITIS ANTISERA AND  
VIRUS FROM PATIENT B. H.

Serum used for Protection	Final Dilution of Virus Injected			
	10 <sup>-4</sup>	10 <sup>-5</sup>	10 <sup>-6</sup>	10 <sup>-7</sup>
Anti-Eastern Type	3/3*	3/3	3/3	3/3
Anti-Western Type	.....	0/3	0/3	0/3
Normal Guinea Pig Serum	.....	0/3	0/3	0/3

\*Numerator represents number of survivors after five days of infection; denominator represents number of mice challenged.

It was concluded that the agent isolated from the brain of patient B. H. was virus of equine encephalomyelitis, Eastern type.

#### DISCUSSION

On the day that B. H. was admitted to Charity Hospital an elderly woman, also of Houma, La., was admitted to a different service in the same institution. Her disease coincided with that of B. H. in time of onset, symptoms, and clinical course, terminating fatally on the same day. No autopsy was performed, and unfortunately the resemblance to our patient was not appreciated until it was too late to secure blood or spinal fluid for study. So far as we have been able to determine, there were no previous illnesses of the same nature reported from that region, and none had developed up to August, 1947.

The evidence of limited outbreaks in

TABLE 2  
RESULTS OF CHALLENGE INOCULATIONS IN MICE IMMUNIZED WITH VACCINE  
FROM VIRUS ISOLATED FROM PATIENT B.H.

Group	Type of Equine Encephalomyelitis Virus Used for Challenge	Dilution of Virus Injected					
		10 <sup>-3</sup>	10 <sup>-4</sup>	10 <sup>-5</sup>	10 <sup>-6</sup>	10 <sup>-7</sup>	10 <sup>-8</sup>
Immunized	Eastern E. E. Virus	0/3*	3/5	5/5	4/5	.....	.....
	Western E. E. Virus	.....	0/3	0/5	0/5	1/5	.....
Controls	Eastern E. E. Virus	.....	.....	0/2	0/2	0/2	0/2
	Western E. E. Virus	.....	.....	0/2	0/2	0/2	0/2

\*Numerator represents survivors after five days of infection with virus used for challenge; denominator represents number of mice challenged.

Three consecutive serum protection tests, performed according to the intraperitoneal technic of Olitsky and Harford<sup>7</sup> showed that mice could be protected against at least 1000 MLD's of the newly isolated virus by guinea pig antiserum to Eastern type equine virus†, whereas antiserum to the Western type of equine virus was without prophy-

Texas and Louisiana suggests the possibility that cases of human infection with this virus may be more frequent than published reports would indicate. Since 1940, 28 human cases diagnosed as encephalitis, of unproved etiology, have been reported to

†The strains employed were supplied by Dr. W. McD. Hammon of the G. W. Hooper Foundation, San Francisco, California.

†Antiserum was sent by Dr. H. Koprowski, Lederle Laboratories, Pearl River, N. Y.



the Louisiana State Health Officer.\* That illnesses diagnosed as postinfection encephalitis are not free from suspicion as possible instances of infection with the virus of equine encephalomyelitis is demonstrated by the observation in Massachusetts that some of the proved cases of infection with equine virus occurred in children convalescent from whooping cough.<sup>2</sup>

Our data concerning the disease in horses are inadequate, but there was certainly no large epizootic during 1946. The virus was recovered from horses in Louisiana in 1944,<sup>3</sup> and many of the potential reservoirs and vectors which have been implicated in studies of the transmission of this infection are found here in abundance. A large outbreak of encephalomyelitis in horses and mules occurred in Louisiana in the summer of 1947, and several human patients suspected of suffering from this infection have been admitted to Charity Hospital. Laboratory studies of these cases are now in progress.

With present methods, a diagnosis of encephalitis due to Eastern equine virus could rarely be established sufficiently early to benefit the patient even if effective means of therapy were known. No distinctive syndrome is yet apparent in the variety of clinical manifestations found among the relatively few examples of this disease previously described in man. As noted above, the early symptoms and relative purulence of the spinal fluid in the patient described here suggested acute bacterial meningitis. The negative smears and cultures of spinal fluid and the sterile cultures of blood did not discourage this view, since it was known that the patient had received penicillin before specimens were collected. The possibility of a viral etiology required consideration when the level of cerebrospinal fluid sugar was found to be normal and when noticeable clearing of the spinal fluid occurred in conjunction with progressively more severe disease.

#### SUMMARY

##### 1. The clinical and pathologic observa-

tions in a case of fatal encephalomyelitis in a 6 year old child from Louisiana are described. Virus of equine encephalomyelitis, Eastern type, was isolated from portions of the brain taken at autopsy. Identification of the virus was established by means of cross-immunization and serum protection tests in mice.

2. Despite the widespread distribution of Eastern type equine encephalomyelitis virus among animals in the United States, this would appear to be the first human case reported since the 1938 outbreak in Massachusetts from which virus has been isolated.

Acknowledgement: The continued interest and helpful suggestions of Dr. Ralph V. Platou are much appreciated by the authors.

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#### FARBER'S TEST IN THE DIAGNOSIS OF CONGENITAL INTESTINAL ATRESIA

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NEW ORLEANS

In 1933, Farber described a simple means to determine patency of the alimentary canal in the newborn infant by examining

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meconium.<sup>1</sup> In his method, meconium is smeared on a glass slide, stained with gentian violet and examined microscopically for cornified epithelial cells and lanugo hairs.

This test is based on knowledge that the embryonic alimentary lumen, from the pylorus to the ileocecal valve, becomes obliterated between the fifth and tenth fetal weeks by proliferation of endothelium and then is recanalized. Rarely, a portion of the solid stage persists as congenital atresia. While in utero, the fetus swallows amniotic fluid, which contains cornified epithelial cells and lanugo hairs during the last two months of gestation. If normal recanalization of the gut has occurred, such formed elements will be found easily in the meconium of the infant. If, on the other hand, atresia persists, they will be lacking. Farber states in his original communication: "Absence of cornified cells is proof that a point of atresia is somewhere present in the alimentary tract."

Here, apparently, is a test of great simplicity which has not been recognized and used to proper advantage. The purpose of this paper is to indicate that epithelial cells are invariably present in the meconium of normal infants and that the test, when done in cases of suspected atresia, has considerable diagnostic and prognostic value.

One hundred full term normal newborn infants with birth weights ranging from 2.5 to 3.75 kilograms were observed during the neonatal period and their meconium examined for lanugo hairs and cornified epithelial cells. None of these infants developed any symptoms or signs of intestinal obstruction. Meconium from each was taken from the center of the excreted mass, smeared on a glass slide, and allowed to dry. The unstained smear was examined microscopically for lanugo hairs. This preliminary examination yielded positive results in 91 cases. The remaining nine were stained after the method outlined by Farber:<sup>1, 2</sup> the slide was immersed in ether for three to five minutes in order to extract fat and then allowed to dry. Next it was stained with Sterling's gentian violet,<sup>3</sup>

washed in water, decolorized with acid alcohol and examined microscopically. In the nine cases in which hairs were not seen on preliminary examination, cornified cells were found readily by this method. The remaining 91 smears were then similarly stained and cornified cells were easily demonstrated to be present in each one. This emphasizes the practical simplicity of the test.

During the period from January 1937 to June 1946, 23 cases of suspected intestinal atresia in the newborn were recorded in this hospital. Farber's test had not been done in any of these. Since June 1946 there have been 24 patients in which the question of patency of the intestinal tract has arisen. Because of increased local interest in Farber's test, it was used in 22 of the latter group.

Comparison between these two groups is of interest. In both periods there was an obvious tendency to rely primarily on radiography as a means of diagnosis. That this faith is not always justified is shown by table 1.

TABLE 1  
ACCURACY OF DIAGNOSIS RELATED TO  
TESTS EMPLOYED

Total Number Patients	Number with Farber's test	Number with Radiography	Number with Correct Diagnosis
Group I (1937-1946) 23 Patients	None	17	7
Group II (1946-1947) 24 Patients	22	15	23

These figures, moreover, demonstrate that when Farber's test was employed and carefully interpreted in relation to other findings, accuracy of diagnosis was greatly increased.

Several individuals from the earlier series deserve mention because they illustrate how Farber's test *might* have yielded information not obtainable in any other fashion.

#### CASE NO. 1

A white male infant, one day of age, began to vomit after feedings and to have abdominal distention. A barium meal was given, and it was noted that the barium churned up and down in the descending portion of the duodenum before passing. On this basis a preoperative diagnosis was made of partial duodenal obstruction due to adhesive



bands. At operation, malrotation was found together with volvulus of the small gut; there was no infarction. Adhesions around the duodenum were released, malrotation and volvulus were corrected. Four days later the child died; necropsy revealed two atretic areas in the jejunum. Had Farber's test been done, such a situation might have been suspected and the outcome altered.

## CASE NO. 2

A colored male infant began to vomit feedings and became distended on the second day of life. Diagnostic workup included plain films of the abdomen, which showed laddering of the gut and gas-filled loops, leading to a diagnosis of jejunal atresia. Slight infection of the umbilicus was noted but was not considered remarkable. At operation generalized peritonitis secondary to omphalitis was discovered, but there was no atresia present. This was confirmed by postmortem examination. Here the diagnosis of atresia could have been ruled out by Farber's test and further consideration of the umbilical infection might have led to the correct conclusion earlier.

## CASE NO. 3

A colored female infant at two days of age began to have continued vomiting after feedings, with gastric distention and retention. Stools were found to contain bile. A diagnosis of atresia of the duodenum was made; at operation the atresia was found one centimeter distal to the pylorus. With presence of bile in the stool, a negative Farber's test in this case could have predicted the exact location of this lesion.

## CASE NO. 4

A six day old colored male infant was admitted with a history of vomiting every feeding and of having passed no fecal matter since shortly after birth. There was complete gastric retention after four hours. A diagnosis of pyloric stenosis was made; operation was delayed while atropine, thickened feedings and other medical management were tried. The baby died and postmortem examination showed not only hypertrophy of the pylorus but associated duodenal atresia. A negative Farber's test would have predicted the futility of medical management.

During the short span of time covered by the second group of cases the personnel in charge of newborn infants were especially alert for any early symptoms or signs which might point to congenital gut defects. As a result, more abnormalities were suspected than were actually encountered. Because of variable abdominal distention, regurgitation of feedings, or difficulties in nursing, such suspicions were carefully investigated for twelve infants. In each of these, Farber's test was done, hairs and cells were found, and congenital atresia was

thereby excluded. Further investigation revealed other causes for the symptoms and operation was not performed. Five patients had multiple obvious external congenital defects at the time of birth and Farber's test was performed to rule out associated atresia before feeding was begun.

In three cases of esophageal atresia with tracheoesophageal fistula, the test proved valuable for excluding associated lower atretic anomalies. In the majority of such infants the esophagus connects with the trachea just distal to the blind esophageal pouch, so that hairs and cells from amniotic fluid easily gain access to the gut. Such a connection is best determined by demonstrating air in the stomach roentgenologically. The presence of air in the stomach in the absence of hairs and cells from the meconium strongly suggests intestinal atresia as an associated anomaly. Hairs and cells were present in the meconium of these three patients and the esophageal operation was undertaken.

Three cases of intestinal atresia were encountered in which hairs and cells were not found in the meconium preoperatively. In one of these, an additional use for Farber's test was found. Serial postoperative examination of meconium stools revealed the presence of cells. Thus, during the immediate postoperative period, when oral feeding of dyes or other marker-substances was undesirable, it was possible to be sure that no areas of atresia had been overlooked and that bowel continuity had been established.

In one infant a clinical diagnosis of sepsis of the newborn was made and Farber's test was omitted (see table 1). At necropsy, in addition to sepsis and peritonitis, congenital malrotation of the gut and a duodenal diaphragm were found. With Farber's test such a condition might have been suspected and successfully attacked surgically.

In the initial group of 23 cases, there was a remarkable preoccupation with radiography as the single most important means of diagnosis. In many published accounts of intestinal atresia, Farber's test is al-

luded to in the discussion but it is infrequently included as a preoperative diagnostic procedure.<sup>4</sup>

#### CONCLUSIONS

1. Cornified epithelial cells were invariably present in meconium of one hundred normal newborn infants. Lanugo hairs were found in 91 per cent of unstained meconium smears. The presence of lanugo hairs and epithelial cells in meconium is evidence of continuous patency of the intestinal tract.

2. This simple examination (Farber's test) should be carried out routinely within the first 48 hours of life when there is any suspicion of gastrointestinal dysfunction. When the results are correlated with symptoms, physical signs, and roentgenologic findings in a given case, accuracy of diagnosis can be materially increased.

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## SOME RECENT EXPERIENCES WITH AMEBIASIS IN CHILDREN\*

MAUD LOEBER, M. D.†

AND

JOSEPH S. D'ANTONI, M. D.††

NEW ORLEANS

Our interest in amebiasis was aroused by the frequency with which it has been encountered among children presenting bizarre and equivocal symptomatology. Seventy-three examples of infection with cysts of *Endamoeba histolytica* were recently identified during a period of less than four months in routine office practice. Recognition of such common occurrence among children "not quite well but not really sick" should make the practitioner more alert to

the possibility that he is dealing with amebiasis, and cause him to be diligent in appropriate diagnostic and therapeutic procedures.

In this infection, as in many others common in the young, remote effects and reflections in other body systems are the rule; among these 73 patients, there were but seven instances of mild dysentery, and only a few more had diarrhea of any significant degree. Symptoms are generally far more suggestive of a low grade systemic infection than of isolated intestinal disease. Three brief protocols will serve to illustrate disturbances which have come to arouse our suspicions; cysts of *Endamoeba histolytica* were recovered from each of these children as a routine procedure, and therapy accomplished relief of the peculiar symptoms, roughly coinciding with disappearance of parasites from the feces.

#### CASE NO. 1

L. M. A., a white girl of 3 years, had been under our care from the time of birth, and aside from occasional mild respiratory infections had always been well. Together with mild constipation, the parents now noted that the child had a capricious appetite, and that her disposition had changed. She seemed unusually irritable, cross, and difficult to manage; she did not enjoy the company of others, and had frequent temper tantrums. Examination showed little other than a peculiar complexion reminiscent of fading suntan, slight enlargement and tenderness of the liver.

#### CASE NO. 2

M. L., a white boy of 18 months, was brought to the office because of recent unexplained poor appetite and restless sleep. He was wilful and highstrung, with seemingly inexhaustible nervous energy, appeared to delight in defiant misbehavior and "baiting" of adults. Particularly distressing to the parents was the child's unaccustomed poor appetite and behavior at mealtime; he took particular delight in refusing morsels he had begged for only a short time before. He indicated the presence of transitory but apparently real abdominal pains. These were often severe enough to awaken him from a sound sleep or disturb play activities he otherwise enjoyed. These pains could not be localized by the child or his parents. While his usual mild constipation did not seem to be affected appreciably by laxative foods or simple medications, close questioning indicated that he had occasional loose mucoid stools, at times even blood-streaked. Complete examination revealed only a peculiar muddy complexion of the skin, moderate enlargement and tenderness of the liver;

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the sclerae and mucosae appeared entirely normal.

#### CASE NO. 3

M. G., a white boy of 3 years suddenly developed mild convulsive seizures which did not fit any recognized pattern. There had been no epilepsy or degenerative disease in the family. Appetite had been poor recently, and the child had had occasional diarrheic stools interrupting a commoner tendency to slight constipation. From his usual sunny, cheerful, outgoing behavior, he had become asullen and retiring child. Physical examination demonstrated only a peculiar sallow complexion, together with a moderately enlarged and tender liver.

Aside from demonstrating cysts of *Endamoeba histolytica* in the fecal examinations, routine laboratory studies failed to reveal significant abnormalities; urinalyses and hemograms showed nothing unusual, serologic tests for syphilis were negative, and no abnormalities in the cephalin-cholesterol flocculation reaction were encountered.

In only one of these children, bowel disturbances had seemed noteworthy to the parents. All, however, had changes in bowel habits, behavior and customary disposition. Abdominal pain dominated the clinical picture in one child, convulsive seizures in the other. In contrast to the varying complaints for which these children were brought to us, the meagre physical findings were essentially similar. Changes after specific therapy for amebic parasites were remarkable.

The general features common to all 73 of these children included changes in appetite, established bowel habits, and personality. Many exhibited disturbed restless sleep, some had occasional diarrheic or loose stools, and in only a few (no more than three) was mucus or blood noted grossly. Nausea, vomiting, low grade fever, headaches insatiable appetite, increased fatigability, weakness, and frequent colds appeared commonly in the listed complaints of parents. Abnormal pigmentation of the skin and equivocal tenderness of a slightly enlarged liver were frequently noted. All of these children were white; 35 were girls and 38 were boys. Three patients were encountered before the first birthday, nine were in their second year, 36 were between

two and six years, and the other 25 ranged in age from six to 12 years.

Justification for this brief review of complaints so ordinarily considered protean lies in the fact that they existed together in patterns so variable as to defy orderly correlation. Only three conclusions seem warranted at present:

1. Alterations in accustomed personality, appetite, and bowel habits were invariably present.

2. A peculiar, though seemingly characteristic "fading suntan" complexion together with a slightly enlarged and tender liver constituted the only distinctive physical signs common enough to be noteworthy.

3. Complaints and abnormal physical signs subsided promptly with appropriate therapy.

We might add that there is need for clarifying further the cause and effect relationships of this disease in children, and that it deserves serious consideration when the diagnostician is faced with a puzzling hodge-podge of complaints that don't seem to fit together.

#### DISCUSSION

Dr. D'Antoni: Enlargement of the liver is an important manifestation of amebiasis in children; its rapid subsidence following therapy with non-absorbed amebicidal agents suggests that it is relatively rarely caused by intrahepatic growth of the parasites, but rather represents a transient toxic hepatitis. In adults, on the other hand, such hepatomegaly together with cysts of *endamoeba histolytica* in the stools would warrant a diagnosis of true amebic hepatitis. I have not any satisfactory explanation for the peculiar discoloration of the skin noted in many of these children, and have been particularly impressed with striking changes in personality and behavior coinciding with institution of therapy.

Not more than 20 per cent of all cases can be identified by examining normally passed stools; material secured after purgation and by sigmoidoscopy is far more satisfactory. We use a well buffered and highly effective saline purgative, and repeat sigmoidoscopy if the first examination is not conclusive.

In practically every family checked to discover the source of infection for these children, at least one adult in the household was found to harbor the parasite. Our studies suggest that it requires about six months of intimate contact for infection to become established in a new individual.

With any form of therapy, cures by our usual

laboratory criteria are notoriously difficult to attain in young subjects such as these. Because of their low toxicity, I have long favored the use of non-absorbed iodine preparations for children. We now give Diodoquin, which contains 63.9 per cent iodine, in full adult dosage to all children who weigh more than thirty pounds; we have no fear of toxicity with this schedule, comprising three tablets (3.2 grains each) three times daily for twenty days.

Dr. Webb: I think the authors have rendered a valuable service in pointing out the frequency of amebiasis in children and emphasizing its bizarre symptomatology, in which diarrhea is so often lacking. I do not believe we have encountered any proved examples of amebic abscess, which must be rare in young patients. Does ulceration of the intestinal tract occur very often?

Dr. D'Antoni: We do not expect it unless there is diarrhea; with rectosigmoidal amebiasis diarrhea usually occurs, and in a few such cases we have seen mild ulcerative lesions. If suspicion of amebiasis awaits the appearance of diarrhea, about 75 per cent of the cases will be missed.

Dr. Sanders: When do you call your patient well?

Dr. D'Antoni: When there is no longer an infection in the intestinal tract; though clinical improvement begins rather promptly after therapy is begun, the patient is not considered to be cured until the diagnostic routine I described has yielded negative results three times over a period of six months.

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## A FAMILY OUTBREAK OF LEAD POISONING FROM STORAGE BATTERY CASINGS

DAVID SPIZER, M.D.†

NEW ORLEANS

Lead poisoning has been recognized for years as an important pediatric and public health problem. Laws prohibiting the use of lead paint on toys and cribs have been followed by a sharp decline in prevalence. Other sources of lead intoxication in children still exist, however, and the following cases illustrate one of these.

The household consisted of a colored family of six who lived in the country in a one room shack with a stove and an open

fire-place in the room. Water was obtained from a deep well. The father, aged 30, the mother, 24 years old, and four children, twins, a boy and a girl three years old, a girl of two years and a boy of one year, all were in good health before this episode. The family income was limited.

The children were breast fed for eight to nine months and had fairly good diets. Growth and development were normal and there was no history of pica. Previous illnesses had been limited to occasional, sometimes bloody, bouts of diarrhea and occasional brief febrile illnesses. No insect or rat poison had been used in the house and the parents were sure the children had had no other access to poison. The family dog went mad four weeks before the children became ill but had not bitten any of the children. The child that died and the one year old child had not played with the dog, but the others had. The father shot the dog but the head was not examined.

### CASE NO 1

J. W., the 23 months old female, was brought to a private physician in Baton Rouge, Louisiana, on December 12, 1946, because of convulsions. The child was first noted to be ill three days previously, the chief symptoms being coryza and diarrhea. On December 11, the day before she was taken to the physician, she seemed to be very nervous, lethargic, weak, could not hold objects in her hands, and had several convulsions. At the time the physician examined the child, she had a temperature of 105.4°. Respirations were 65 and she was having severe convulsions. The patient was immediately referred to a local hospital but died on admission there. No information was available on physical or laboratory findings at that hospital.

### CASES NO. 2 AND 3

Bobby W. and Betty J. W., the 3 year old twins, had almost identical stories. They were brought to Charity Hospital at New Orleans on December 13, 1946, the day after the death of the younger sister, chiefly because of this fact. The complaints at this time were limited to drowsiness, anorexia, irritability, and mild diarrhea, all of two days' duration.

On admission neither child had fever, the temperatures being 98.0° and 98.4°. Physical examination of both children revealed no abnormalities, other than the drowsiness and irritability. There was no papilledema, stiffness of the neck or other signs of disorder of the nervous system.

Because of the familial character of the outbreak and the history of diarrhea, the tentative

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TABLE 1  
LABORATORY DATA

	Betty J. W. 3 years	Bobby W. 3 years	Smiley W. 11 months
BLOOD			
RBC	3,350,000	4,900,000	3,830,000
Hgb.	9.0 gms.	11.2 gms.	10 gms.
WBC	10,500	12,900	5,850
PMN	39	49	55
L	57	45	38
M	1	0	3
E	3	6	4
SMEAR	Basophilic stippling present, 3 to 4 per high power field.		Basophilic stippling present, but rare.
URINE	Completely negative except for one plus reduction of Benedict's, which disappeared in all three cases on second examination.		
SEROLOGIC TEST FOR SYPHILIS	Negative	Negative	Negative
BLOOD SUGAR	89	78	----
SPINAL FLUID	----	Clear Pressure 100 mg. No cells Protein 50 mg. Sugar 133 mg. Chloride 708 mg. ----	----
X-RAY OF LONG BONES	All three cases showed marked linear increase in density in metaphysis adjacent to epiphyseal line.		

diagnosis at admission was possible shigellosis.

The laboratory data in these two children and the younger child are summarized in table 1.

With the discovery of stippled red blood cells the diagnosis of lead poisoning came to the fore. Further confirmation was obtained from the x-ray findings.

Because of the absence of serious symptoms in the children the need for immediate treatment as soon as lead poisoning was suspected was not appreciated. Three days after admission, however, Betty J. W. had a generalized convulsion lasting five minutes and followed by cyanosis. A second convulsion of the same duration appeared an hour later. There were no further convulsions subsequently. Phenobarbital, 30 mgms., was given for sedation.

Treatment directed at immobilizing the lead was begun promptly after the convulsion. The children were given a high calcium diet with a high phosphorus to calcium ratio. This included a quart of milk a day. Vitamin D was given in the form of calciferol, 5000 units daily. The children also received calcium lactate 0.65 grams t.i.d. and sodium citrate 2 grams t.i.d.

The other child never had any convulsions. The drowsiness and irritability improved steadily in

both children and were completely absent 12 days after admission. They were discharged, apparently in good health, on December 28 after a total hospital stay of 15 days.

#### CASE NO 4

Smiley W., the 11 month old male, actually was the first in the family to become ill. The onset had been on December 8 with fever, irritability, vomiting, and diarrhea. He had ten to twelve watery bowel movements per day which contained quantities of mucus but no blood. Fever and diarrhea persisted until December 12, when he was hospitalized in Baton Rouge, Louisiana, chiefly because his sister had died that day. The patient had a convulsion the following day, but vomiting and diarrhea ceased in the hospital. He continued to be very irritable, however, and required sedation. A spinal tap was negative except for a slight elevation of pressure. No further laboratory data were available.

He was referred to Charity Hospital at New Orleans on December 18, after a diagnosis of lead poisoning had been made for the other children. The only positive findings at this time were marked irritability and pallor. There was no papilledema.

His treatment was essentially the same as that for his older siblings but sedation had to be carried out for a longer period of time because of his

marked irritability. No convulsions appeared in this hospital and his improvement was steady. He, too, was discharged on December 28, apparently in good health, after a total hospital stay of ten days.

#### COMMENT

The first clue to correct diagnosis in these cases was the finding of generalized stippling of the red blood cells. Credit for making this finding goes to a third year student who reported it promptly to the house physician. With the probability that the children were suffering from lead poisoning in mind, the parents were queried further regarding possible sources of the metal. No painting had been done in the house, there was no use of any pipe for drinking water, the children had no lead toys, and they did not chew on the furniture. Specific inquiry was then made regarding the fuel used in the fireplace and stove and it came to light that storage battery casings were being used almost exclusively. The father stated that they had used casings occasionally during the past three years when they could not obtain wood, but not for more than a day or two at a time. However, this winter they were unable to obtain wood and casings alone were burned for three consecutive weeks. The casings were burned in a wood stove in the room in which the children slept. Unfortunately no smears were made of the parents' blood but they had no symptoms of lead intoxication.

The first report of an epidemic of lead poisoning from the burning of battery casings was made by Williams, Schulz, Rothchild, Brown, and Smith<sup>1</sup> in 1933. They described 40 cases which occurred in poor homes in the city of Baltimore within a period of two months. Investigation disclosed that intermittent lead poisoning had begun to occur in the winter of 1930-31, when, with the economic depression reaching new low levels, junk dealers allowed poor persons to secure, free or at small cost, the casings of discarded storage batteries for fuel. These casings, which carried a considerable deposit of lead salts, burned freely and were an excellent source of heat, despite the penetrating and unpleasant odor

produced. It is interesting to note that the original suggestion that storage battery casings might be at fault came from the uncle living in the house where the first child case was discovered. Cooperative public health educational efforts as a result of this epidemic apparently resulted in essentially eliminating the hazard in Baltimore. Several other cities took heed at the time and also carried on educational campaigns concerning this danger.

Other series of cases<sup>2, 3</sup> of lead poisoning from this source have been reported and it has been emphasized by Bourne,<sup>4</sup> particularly, that increased prevalence among negroes was probably due to their generally lower economic status.

A point of interest is the high proportion of children among all the series reported. At least two explanations are offered—one that children are in the house more than adults and therefore have quantitatively greater exposure, and the other, that there is proportionally greater absorption in children of inhaled lead fumes. McKhann<sup>5</sup> cites animal experimentation to support the thesis that the young of a species are more susceptible to lead intoxication than adults. Whatever the explanation, the greater incidence in children justifies extra precautions and continued educational efforts to prevent a serious and often fatal disease.

#### SUMMARY

1. The source of four cases of lead poisoning in one family was found to be the use of storage battery casings as fuel.

2. One patient died and the other three children had evidence of lead encephalopathy manifested by convulsions in two and irritability and drowsiness in one.

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## PEDIATRIC PROGRESS IN LOUISIANA

Prominent among developments in this specialty during the past twelve months was the formal reactivation of the Louisiana State Pediatric Society. Members have contributed generously to the annual program of the State Medical Society, as attested by a number of articles included in this issue. The group has met on two other occasions and has recently decided to hold regular meetings quarterly hereafter. An excellent program has already been planned for the next annual session at Monroe.

Dr. Sidney S. Chipman has recently come to Louisiana to serve as a member of the Pediatric staff at Louisiana State University Medical School and as pediatric consultant for the State Health Department. Both Tulane and L. S. U. Medical Schools are conducting many postgraduate activities, and at present have twenty-one graduate physicians enrolled as residents at Charity Hospital or as departmental fellows in training for completion of specialty Board requirements.

Through the cooperation of the State Health Department, the United States Children's Bureau, and the Board of Administrators of Charity Hospital, funds have been secured to permit expansion of facilities for care of premature infants. New construction, additional personnel and equipment bid fair to make this revised unit at Charity Hospital in New Orleans one of the largest and finest of its kind anywhere. An integral part of the program here is a plan for establishing a training center for graduate physicians and nurses. It is anticipated that teaching and research activities will lead directly to important advances in methods of caring for premature infants.

A new pediatric division at Hotel Dieu was formally dedicated on March 18, 1947, incorporating complete facilities for the care of 43 infants and children. On October 15, a pediatric ward was added at Foundation Hospital. A new pediatric wing is included in the Baton Rouge General Hospital now under construction; in the same city there are increased facilities for the care of children in the new Lady of the Lake Sanitarium. Appropriations have been made for establishing a special school for educable victims of spastic paralysis at Alexandria; this facility is now ready to receive its first pupils.

Collection of data for the Study of Child Health Services, sponsored by the American Academy of Pediatrics, is practically complete for Louisiana. We all owe a debt of gratitude to Dr. Clarence Webb, State Chairman for this study, to Dr. Verre Simpson, who served as Executive Secretary, and to numerous organizations and indi-

viduals interested in child welfare, without whose vigorous support this difficult project could not have been completed. Analysis of all schedules is now in progress, and Dr. Webb has appointed an Action Committee to interpret results and make specific critical recommendations. Their reports should appear in this Journal during the next few months.

Space does not permit a complete review of progress in pediatrics here; the foregoing brief notes serve only to point out a few praiseworthy activities which illustrate prevailing progressive attitude of workers in this field. Accomplishments within such a brief period augur well for the future of our state's richest natural resources—its infants and children.

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#### NEONATAL DEATHS

Careful pathologic study of causes for death in prematurely born infants is the keystone on which effective clinical programs to reduce unnecessarily high mortality rates may be based. Conscientious investigators now have serious qualms about accepting prematurity alone as an adequate explanation for death. Continued improvement in survival rates for these small infants attests the fallacy of many empirically drawn criteria used to differentiate the premature from the mature infant or the previable from the viable fetus. There is general agreement that no fool-proof criteria exist for such differentiations. Still, in all parts of the country, "prematurity" alone often appears—and is ordinarily accepted—as an adequate cause of death. Certainly, incomplete development is an important contributory factor, but in the majority, specific lesions can be disclosed. Failure to discover adequate anatomic bases for death in about 10 per cent of *mature* newborns tempts no one to inscribe "mature infant" as a cause on death certificates. Continuance of the practice of considering prematurity as more than a contributory factor calls to mind the classical head-in-sand performance of the ostrich.

Were it possible to carry out complete

studies of all deaths among premature infants in the meticulous manner reported by Dr. Arey in this issue, there is no doubt that many fatalities now listed under "prematurity" or "cause undiagnosed" would be properly classified. Such studies as his should serve as a real stimulus for improving all aspects of our current programs directed at reduction of mortality among premature infants. We are in agreement with Potter, that at least 40 per cent of neonatal deaths are preventable on the basis of present knowledge—further knowledge and improved facilities can be expected to increase this percentage. This in turn depends on *more interest* and *more support* of more people in *more healthy infants*. Prevailing high death rates among our smallest citizens are not necessarily inevitable.

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#### BEHAVIOR DISORDERS AND PHYSICAL DISEASE

Conduct disturbances are among the most common problems encountered by physicians who care for children. Their occurrence in the presence of physical disease is well recognized and the interesting report by Loeber and D'Antoni in this issue provides another apt illustration of this association.

It is important to bear in mind, however, that the genesis of such behavior disorders, mild or severe, is not easily explained. Those who are interested in psychosomatic medicine have repeatedly noted that psychic disorders both in children and adults disappeared after cure of physical disease, and, vice versa, that elimination of underlying psychic disturbances often resulted in disappearance of symptoms suggesting physical disease. It should not be inferred, therefore, that the occurrence of behavior disorders in children with amebiasis necessarily implies a specific causal relation. Parents who have been worried about a child's behavior, and whose worries in turn accentuate the behavior disturbances, may derive more psychologic benefit from being told that a definite diagnosis of physical disease has been made than from spe-



cific drug therapy given to the child. In an area of the country where parasitic infections are common and often quite symptomless, it is extremely difficult to relate minor changes in symptoms to presence or elimination of particular parasites.

The need for controlled studies to elucidate this relationship further is emphasized by the high prevalence of infection with cysts of *Endamoeba histolytica* in children, shown by these authors.

## ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

***An informed profession should be a wise one.***

### ANNUAL REPORT OF COMMITTEE ON RURAL HEALTH

Our Rural Health Committee is now in its third year and has been very active since its formation, three members of which attended meetings in Chicago.

Several meetings have been held with members of Rural Health Committee of the Farm Bureau in Louisiana and there has been organized an advisory council to the Farm Bureau, which council is composed of the following organizations.

- Louisiana State Medical Society.
- Louisiana State Medical Auxiliary.
- Louisiana State Dental Society.
- Louisiana State Department of Public Welfare.
- Louisiana State Department of Education.
- Louisiana State Board of Health.
- Louisiana Parent-Teachers Association.
- Louisiana Federation of Women's Clubs.
- Louisiana Tuberculosis Association.
- Louisiana Cancer Society (Division of American Cancer Society).
- Louisiana Society for Crippled Children.
- Louisiana Farm Home Administration.
- Louisiana Agricultural Extension Service.
- Blue Cross Association.
- Louisiana Physician's Service.
- Louisiana State Nurses Association.
- Louisiana Home Demonstration Council.
- Louisiana Hospital Association.
- Louisiana Press Association.
- Louisiana Department of Institutions.
- Louisiana Experiment Station.

Associated Women of Louisiana Farm Bureau.

Louisiana Conference of Social Welfare.  
Louisiana Farm Bureau.

Other statewide organizations or agencies which have a direct interest in rural health may be elected to membership by a vote of a majority of the members of the council.

Members at large may be elected by a majority vote of the members of the council.

A meeting was held in Baton Rouge June 22. Constitution and by-laws were drafted, in which the purpose is stated as follows:

"It shall be the purpose of the council to discuss problems relating to the health of the rural people of Louisiana, to prepare recommendations for the betterment of rural health as can be agreed upon by a majority of the members present at regular or special meetings, to advise and make recommendations to the Board of Directors of the Louisiana Farm Bureau with regard to their policies and programs for the betterment of rural health, and to sponsor the organization of local health councils."

At the State Medical Society meeting Mrs. T. R. Tomlinson, Chairman of Rural Health of Farm Bureau, was present and addressed the House of Delegates.

On Sunday, July 13 the American Academy of General Practice of Louisiana was organized. Dr. J. P. Sanders, a member of the Louisiana Rural Health Committee was elected president. Dr. Guy Jones was elected president-elect, Dr. D. B. Barber,

vice president and Dr. M. C. Wiginton a member of the Board of Directors.

The Louisiana State Medical Society has organized the Blue Shield Insurance Plan which is working with Blue Cross, and is now being offered to the rural areas.

A survey has been made in Louisiana of the hospital facilities of the state in conformity with requirements of the Hill-Burton Bill.

Assurance has been obtained that the medical schools in Louisiana will advocate a course in general practice and our hospitals will offer residencies in general practice which we hope will promote more and better general practitioners for rural areas.

On October 23 and 24 there was held in New Orleans the Southern Regional Conference of the American Medical Association Council on Medical Service. The Committee on Rural Health attended and on the night of the 23rd a banquet was held for found table discussion on Rural Health. This was well attended.

Respectfully submitted,

Guy R. Jones, M. D., A. A. G. P.

Chairman, Committee on Rural Health

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## REGIONAL CONFERENCE OPPOSES PROPOSED CONTROL OF MEDICINE BY GOVERNMENT

Keynoting the Southern Regional Conference meeting held in New Orleans recently was the unanimous opposition of the medical profession to a federal program of socialized medicine. The two-day Southern Regional Conference was sponsored by the Council on Medical Service of the American Medical Association in cooperation with the Council on Medical Service and Public Relations of the Louisiana State Medical Society.

"We are bitterly opposed to the socialization of medicine because in every country where the plan has been instituted it has brought an inferior grade of medical care," Dr. George F. Lull, Secretary and General Manager of the AMA and former deputy

surgeon general of the U. S. Army, informed the conference.

Dr. Lull said that through the institution of prepaid medical and surgical care plans in the country any government attempt at socialized medicine can be staved off.

Dr. James McVay, conference chairman and chairman of the AMA's Council on Medical Service, explained the purpose of the conference and stated, "The AMA does not fight proposals for socialized medicine, we merely promulgate other methods of medical care which have proven superior.

"In voluntary prepayment plans such as the Louisiana Physicians Service, patients may choose their own doctor. A patient-physician relationship is firmly established. Under a federal program the patient would lose his identity. He would go to any doctor at a bureau. The patient would lose his individuality.

"One of the primary purposes of the conference is to plan for prepaid medical care for everyone in the country through a method of budgeting medical expenses."

Both Drs. Lull and McVay praised the Hill-Burton program, which has made extensive surveys into hospital and health facilities in U. S. rural and urban areas.

Dr. McVay came to New Orleans from Kansas City and Dr. Lull from AMA headquarters in Chicago.

The conference fostered the interchange of ideas on Public Relations, Prepayment Medical and Surgical Care Plans, Industrial Health and Rural Health.

The portion of the program devoted to Public Relations was headed by Henry Johnson, Public Relations Director for the Medical Society of Virginia. Five panel discussants actively participated in the public relations program and presented papers and answered questions expounded by members attending the conference.

Dr. Charles R. Henry of Little Rock, Arkansas, was moderator for the portion of the conference devoted to the discussion of prepayment medical and surgical care plans. More than 65 plans are now sponsored by either a state or county (parish) medical society, providing a medium where-



by more than seven million persons may prepay the cost of their anticipated medical bills.

Inauguration of a medical school program on prevention and treatment of diseases related to atomic energy was urged by Dr. Jean Felton, health department superintendent at the University of Chicago laboratory at Oak Ridge, Tennessee, atomic bomb plant. Dr. Felton participated in the Industrial Health portion of the conference. Dr. Raymond Hussey of Detroit, vice-chairman of the AMA Industrial Health Council, was moderator at the Industrial Health session.

The general practitioner was described as "the work horse of American Medicine" by Dr. J. Paul Jones of Camden, Alabama, member of the AMA's Rural Medical Service Committee and moderator for the Rural Health portion of the conference program.

Dr. Jones stressed the following as "pressing" rural health problems.

1. Hospital facilities and health centers.
2. Voluntary prepayment plans.
3. Nursing needs of rural communities.
4. Methods of bringing and holding doctors and dentists in rural areas.
5. Health councils as an agency for promoting rural health.
6. Medical care for low income groups.

A rural health panel discussant, Dr. William C. Chaney of Memphis, Tennessee, emphasized the fact that "People would like to see the physician a little more human; human enough to come into their homes when they are seriously ill. After all, people can die at home," he asserted.

Turning to what he labeled as a serious problem facing the medical profession today, Dr. Chaney said:

"The startling fact that our national government in 1946 spent \$75,000,000 of the taxpayers' money to spread propaganda favoring the government control of the practice of medicine should bring every physician, dentist, pharmacist and nurse to his feet with the shocking realization that American medicine . . . may soon come to an end unless we do something about it."

The conference was attended by delegates from Louisiana, Mississippi, Alabama, Arkansas, Oklahoma, Tennessee and Texas.

The Council on Medical Service and Public Relations of the State Society handled local arrangements for the conference. Members of the Council are: Dr. A. V. Friedrichs, Chairman; Dr. P. T. Talbot, Dr. Daniel J. Murphy, all of New Orleans; Dr. John G. Snelling of Monroe; Dr. O. B. Owens of Alexandria and Frank Lais, Jr., Executive Director, New Orleans.

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### STATE PREPAYMENT PLAN CELEBRATES FIRST ANNIVERSARY

Louisiana Physicians Service celebrated its first anniversary on November 1. The first prepayment surgical and obstetrical care plan contracts issued by the company became effective November 1, 1946.

During the past year the company has been able to enroll nearly 20,000 individuals. In the same period, 1,965 claims were serviced. In the servicing of these claims the plan has paid to doctors throughout Louisiana in excess of \$95,000.00 in claims for services rendered to LPS subscribers and their dependents.

Greatest utilization has been on the following listed services: Tonsillectomy and adenoidectomy; obstetrics, appendectomy, hysterectomy, anesthesia and x-ray.

The plan spreads the costs of medical care over a long period of time and among individuals through the application of the insurance principle. Through this medium a person can budget his anticipated medical needs—his anticipated doctor bills by paying a small amount each month into a common fund on a prepayment and post-payment basis—just as he would purchase any tangible asset on a part-payment or installment basis.

The subscriber may choose his own doctor and the doctor remains free of bureaucratic restrictions on his methods of treatment. It is anticipated that plans of this type throughout the nation will be an ally and instrument in the physicians'

hands in preserving the practice of medicine as it is known today and will forever kill the threat of socialization of medicine.

Dr. H. Whitney Boggs, Secretary-Treasurer of the plan recently stated that "desires often are more expensive than needs. The doctor gets only 13 cents out of each dollar the public spends for health. The remainder goes to medicine manufacturers, leaders of health cults, druggists, hospitals and others."

Dr. Boggs pointed out that people spend more for cigarettes, cosmetics, liquor and other luxury items than for doctor bills. But because medical expenses come all at

once and are not always expected, many cannot pay them. More than 41 per cent of the population is in an income group which does not permit them to meet major doctor bills.

The remaining problem remains for an all-out presentation of the plan to the general public throughout Louisiana. We request that each physician take a personal interest in the presentation of his plan and encourage his patients to inquire about its protection. Within a few weeks printed material will be available and we ask that as many physicians as possible contact our office for a supply to be included in next mailing of monthly statements to patients.

## TRANSACTIONS OF ORLEANS PARISH MEDICAL SOCIETY

- December 8, Orleans Parish Medical Society  
8 p. m.
- December 9, Orleans Parish Radiological Society, 7:30 p. m.
- December 10, Woman's Auxiliary, Orleans Club,  
3 p. m.  
Touro Infirmary Staff, 8 p. m.
- December 11, Clinico-pathologic Conference,  
Touro Infirmary, 12 noon.
- December 15, Hotel Dieu Staff, 8 p. m.
- December 16, I.C.R.R. Hospital Staff, 12:30 p. m.  
Charity Hospital Medical Staff,  
8 p. m.
- December 17, Charity Hospital Surgical Staff,  
8 p. m.
- December 18, New Orleans Hospital Dispensary  
for Women and Children Staff,  
8 p. m.  
Veterans Administration Hospital  
Staff, 8 p. m.
- December 19, Lakeshore Hospital Staff, 8 p. m.
- December 22, DePaul Sanitarium Staff, 8 p. m.
- December 23, Baptist Hospital Staff, 8 p. m.
- January 2, Foundation Hospital Staff, 8 p. m.
- January 5, Board of Directors, Orleans Parish  
Medical Society, 8 p. m.
- January 6, Eye, Ear, Nose and Throat Staff,  
8 p. m.
- January 7, Mercy Hospital Staff, 8 p. m.
- January 8, Clinico-pathologic Conference,  
Touro Infirmary, 12 noon.
- January 12, Installation Meeting, Orleans Parish  
Medical Society, Jung Hotel,  
7:30 p. m.

### NEWS ITEMS

The following members of the Society participated in the program of the Southern Psychiatric Association in Birmingham, October 13-14:

Dr. John W. Bick, Jr., spoke on the "Adjustment Problems in the Modern Woman"; Dr. Hunter Harris read a paper prepared by Dr. H. O. Colomb on "The Transference Mechanism in Medical Practice"; and Dr. Theo. A. Watters spoke on the "The Ego and the Eye."

Dr. Walter Otis, who also attended this meeting, was installed as vice-president of the organization.

Dr. Theo. A. Watters recently attended the annual conference of the Menninger Foundation at Topeka, Kansas. Before returning to New Orleans, Dr. Watters visited the Winter Veterans Hospital, where the largest training program for psychiatrists in the world is going on—120 being trained at the present time.

Dr. Ruth M. Shushan has just returned from New York where she was a member of the first class in cytologic diagnosis of cancer, given by Dr. George Papanicolaou at Cornell University Medical College.

Dr. Edmond Souchon was recently elected a fellow in the International College of Surgeons.

Dr. Charles L. Eshleman was elected president of the medical staff of Foundation hospital on September 26. Other officers elected were: Dr. A. Seldon Mann, vice-president; Dr. Robert C. Lynch, secretary-treasurer; Drs. Thomas Findley,



L. S. Meriwether and I. Mims Gage, members of the executive committee.

Dr. E. J. Richard was re-elected as head of the independent unit staff at Charity hospital on September 24. Dr. Blaise Salatich was elected secretary. Heads of departments named were: Dr. F. F. Boyce, surgery; Dr. Adolph Jacobs, obstetrics; Dr. George Battalora, orthopedics; Dr. Monroe Wolf, urology, and Dr. J. Roeling-Hanley, orthorhinolaryngology. Three staff members named were: Drs. John F. Oakley, N. J. Tessitore and E. L. Zander.

The following officers of the Charity Hospital Visiting Staff were elected at the annual meeting of the Staff held October 2: Dr. P. H. Jones, Jr., president; Dr. J. D. Rives, vice-president; Dr. Nathan Polmer, secretary; Drs. John Oakley, Edgar Hull, Conrad Collins and E. J. Richard, members of the medical advisory committee.

At a recent meeting of the Metairie Foundation Hospital Dr. Joel B. Gray was elected president of the staff. Other officers elected are as follows: Dr. Louis J. Gehbauer, vice-president; and Dr. Wallace C. Beil, secretary-treasurer.

## LOUISIANA STATE MEDICAL SOCIETY NEWS

### C A L E N D A R

#### PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

#### RAPIDES PARISH MEDICAL SOCIETY

The Rapides Parish Medical Society is celebrating on January 10, 1948 their "Founders Day" by putting on a top-notch full day's program under the name of "Founders Day Forum". There are to be scientific papers beginning at 10:00 a. m., a luncheon at 12:15 p. m. and an afternoon session which will end at 4:30 p. m. Appearing on the program are some of the outstanding specialists and teachers on the staffs of Louisiana State University and Tulane medical faculties. In the evening the annual banquet will be held and the group will be addressed by an outstanding guest speaker. The Bentley Hotel, Alexandria, is the site for the all day program.

Certainly the doctors of Rapides Parish and the members of the arrangement committee are to be congratulated on this unique and outstanding program. All members of the profession should make plans now to attend and take advantage of this scientific, cultural and social opportunity—a real red letter day in medical progress.

#### SIXTH DISTRICT MEDICAL SOCIETY

Members of the Sixth District Medical Society held their semi-annual meeting at East Louisiana State Hospital in Jackson, November 7. Members

present were guests of the Hospital at supper and then retired to a scientific program.

Dr. Charles E. Sturm of the Hospital staff presented a paper on shock therapy. Dr. Charles S. Holbrook of New Orleans spoke on statistics pertaining to shock therapy. Fractures of the elbow were discussed by Dr. I. L. George of Baton Rouge.

#### NATIONAL CONFERENCE OF COUNTY MEDICAL SOCIETY OFFICERS

The Grass Roots Conference of the National Conference of County Medical Society Officers, the purpose of which is to develop a working partnership between the American Medical Association and all physicians, will be held at the Statler Hotel in Cleveland, Ohio on January 6. Subjects to be discussed are: 1. The General Practitioner; How to Create More of Them for the Future Need of the Country; 2. Upholding the Prestige of the General Practitioner; 3. The General Practitioner and Community Leadership. Hotel reservations should be requested through Dr. David Chambers, Chairman Hotel Committee (A.M.A.), 511 Terminal Tower, Cleveland 13, Ohio.

#### SIXTH DISTRICT AMERICAN ACADEMY OF GENERAL PRACTITIONERS ORGANIZED

An organization meeting of the American Academy of General Practice in the Sixth District

was held November 7, at the East Louisiana State Hospital in Jackson. The meeting was held immediately preceding the semi-annual meeting of the Sixth District Medical Society.

Officers elected by the group are as follows: Dr. M. C. Wiginton of Hammond, President; Dr. A. L. Lewis of Amite, Vice-President; Dr. Charles J. Wise of Angola, Secretary-Treasurer. Arrangements for the election of eight directors to the board of the Sixth District A.A.G.P. were completed and the board is expected to function as such by the time of the next meeting. It is anticipated that each organized medical society in the district will have one representative on the board.

Dr. D. B. Barber of Alexandria, Vice-President of the State A.A.G.P. talked briefly on the benefits of the general practitioner becoming a member of his district organization. Dr. Joel Gray of New Orleans spoke on the Constitution and By-Laws. Dr. O. W. Topp, recently elected President of A.A.G.P. of the Seventh District, talked on the organization of that district.

Dr. Wiginton reported approximately thirty members enrolled from the Sixth District.

#### PUBLIC RELATIONS PROGRAM PLANNED BY SHREVEPORT SOCIETY

Reports are that the Shreveport Medical Society through its Public Relations Committee expects to establish an active Public Relations program in the Shreveport area right after the first of the year.

A luncheon meeting was recently held in Shreveport to formulate tentative plans for the establishment of the program in cooperation with the proposed Public Relations program of the State Society. Shreveporters interested in Public Relations attending the meeting were: Dr. Jos. E. Heard, President of the local society, Dr. R. Denman Crow, Dr. W. G. Wells, Dr. A. A. Herold, Dr. H. Whitney Boggs and two members of the Public Relations Committee, Dr. J. R. Stamper and Dr. J. P. Sanders. Mr. Frank Lais, Jr., Executive Director of the Council on Medical Service and Public Relations, also attended and represented the Council.

Mr. Lais advised the group that numerous prepared recordings are available from AMA headquarters in addition to numerous other mediums of promoting public relations. He suggested the establishment of speaker bureaus in order that the doctor may present to the public his opposition to the socialization of medicine. Dr. Boggs advised the group that it was his belief that the Shreveport Chamber of Commerce would assist in the presentation of their program.

#### PREPAYMENT PLAN EXPLAINED TO SHREVEPORT AUXILIARY

An open forum, sponsored by the Woman's

Auxiliary of the Shreveport Medical Society, was held recently in the State Exhibit Building in Shreveport. Features, benefits and economics of a prepaid medical insurance plan were explained by three officers of Louisiana Physicians Service: Dr. H. Whitney Boggs, Secretary-Treasurer, Dr. O. B. Owens, President, and Frank Lais, Jr., Executive Director.

Dr. Boggs said that medical economics involves persons in the low-income brackets, who have to struggle to satisfy their economic wants. Economics, he stressed, is a study of a person's needs and/or his desires. By spreading financial risk, the prepaid medical plan makes it possible for persons to meet their medical obligations.

Pointing out that Louisiana Physicians Service spreads medical costs over a long period of time and among individuals, the speakers declared that it provides low-cost service and that it is the answer to threats of socialized medicine.

Dr. Owens asserted that over a long period of time, the medical profession has been threatened with the possibility of having forced upon it a federal bureaucratic control, or dictatorial system, of the distribution of medical care. Heeding this menace, the doctors of the nation have organized their own plans, advocating free enterprise.

#### NEWS ITEMS

Dr. Robert A. Katz has returned from England and the Continent, where he has been for the past two months. While there, he reported on his researches on arteriosclerosis.

On November 2 and 3, he presented in Chicago, to the American Society for the Study of Arteriosclerosis, two addresses: "The Status of Arteriosclerosis in Europe" and "Intravenous Ether, a New Approach to the Therapy of Arteriosclerosis."

#### INTERNATIONAL COLLEGE OF SURGEONS

At the Twelfth Assembly and Convocation of the United States Chapter, International College of Surgeons, held in Chicago on October 3, the following Louisiana doctors were among the 810 surgeons inducted into the College:

**FELLOWS:** Peachy Ridgway Gilmer, M. D., Shreveport; John A. Hendrick, M. D., Shreveport; Claude A. LaRue, M. D., Shreveport; Frank C. Shute, Jr., M. D., Opelousas; Edmond Souchon, II, M. D., New Orleans; John Wm. Faulk, Sr., M. D., Crowley; Wilton Paul Duncan Tilly, Sr., M. D., New Iberia.

**ASSOCIATES:** Charles V. Hatchette, M. D., Lake Charles; William V. Garnier, M. D., Bastrop; Charles McVea, M. D., Baton Rouge; William Henry Roeling, M. D., New Orleans; William McGinty McBride, M. D., Alexandria.

**AFFILIATES:** Jay W. Cummins, M. D., Monroe; Joseph A. Vella, M. D., New Orleans.



**MATRICULATE:** Richard Denman Crow, M. D., Shreveport.

#### COLLEGE OF AMERICAN PATHOLOGISTS

The first general meeting of the College of American Pathologists was held in Chicago on October 27. A dinner meeting was held at the Drake Hotel after which there was formal introduction of members of the College at a meeting in the John B. Murphy Memorial Auditorium. Included were the following physicians from Louisiana: Dr. John L. Beven, Baton Rouge; Dr. Willis P. Butler, Shreveport; Drs. S. H. Colvin, Charles E. Dunlap, George H. Hauser, Russell L. Holman, Edwin H. Lawson, Aldea Maher, Emma S. Moss and Phillip Pizzolato; all of New Orleans.

The objects of this new organization are to (a) foster the highest standards in education, research, and the practice of pathology, (b) through study, education, and improvement of the economic aspects of the practice of pathology to advance the science of pathology and to improve medical laboratory service to physicians, to hospitals and to the public, (c) to maintain the dignity, precision and efficiency of the specialty of pathology for the service of the common good.

#### SCIENTIFIC EXHIBIT AWARD

Scientific exhibit, entitled "The Etiologic Agents of Mycotic Infections; Laboratory Methods of Identification and Classification" prepared by Drs. Albert L. McQuown and Emma S. Moss, of New Orleans, merited a silver medal at the 1947 meeting of The American Society of Clinical Pathologists held in Chicago October 27-30.

#### NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

The National Society for the Prevention of Blindness will hold its 33rd Annual Meeting on December 12, in the Russell Sage Foundation Building, 130 East 22nd Street, New York City.

The principal speaker will be Dr. C. E. A. Winslow, Editor of the *American Journal of Public Health*. Dr. Winslow's subject will be "Prevention of Blindness in the Public Health Program."

Activities of the National Society for the Prevention of Blindness during the past year will be reviewed by Dr. Franklin M. Foote, Executive Director and Mason H. Bigelow, President of the Society, will preside.

#### EIGHTH ANNUAL CONGRESS ON INDUSTRIAL HEALTH

The Council on Industrial Health will hold its Eighth Annual Congress on Industrial Health in the Cleveland Auditorium, Cleveland, on January 5-6, 1948. These dates immediately precede the Interim Session of the American Medical Association,

which will be held in the Auditorium on January 7-8. General practitioners supply a large part of the medical services which workers receive through industry, and they are cordially invited to attend these industrial health sessions. The program of the Congress is being constructed with general practitioners in mind and will include discussions of first aid and emergency services in industry, physical examinations, administrative practices, applied physiology, aviation medicine, radiation medicine and practical expositions of occupational disease management, traumatic surgery and rehabilitation. Since full use of medical services in industry depends on support from management and the worker, the essential relationships will be discussed. Industry needs medicine as a practical ally and to promote human relations. The Industrial Health Congresses are intended to further these objectives.

#### EYE SPECIALISTS OF THE AMERICAS TO MEET IN HAVANA

Plans have been announced for the Third Pan-American Congress of Ophthalmology, which is to be held in Havana, Cuba, January 4-10, 1948. It is anticipated that about 1,000 eye specialists will attend the sessions at the University of Havana School of Medicine.

A program of more than forty formal papers has been arranged, with speakers divided about equally between physicians of the Northern half of the hemisphere and those of the Latin American countries. Papers presented by English-speaking ophthalmologists are to be discussed by their colleagues who speak Spanish, Portuguese or French, and the papers in the Latin languages will be discussed by members of the English-speaking contingent. During the presentation of each paper, slides bearing resumés of one other language will be shown, in order to facilitate understanding by those who are unfamiliar with the language used by the speaker.

Topics on which the eye physicians will exchange information cover a wide range. They include operations for cataract, glaucoma and crossed eyes, parasites that attack the eyes, hazards to the eyes in industry, effects of high blood pressure, syphilis and certain tropical diseases on the eyes, tumors, sulfonamide and penicillin treatment, and diseases peculiar to high altitudes of such countries as Peru and Bolivia.

#### MIDWINTER SEMINAR IN OTOLARYNGOLOGY AND OPHTHALMOLOGY

The University of Florida Midwinter Seminar in Otolaryngology and Ophthalmology will be held at the Flamingo Hotel in Miami Beach, beginning on January 12-17, 1948. Registration fee will be \$25.00.

Distinguished lecturers for the courses in Otolaryngology include Drs. Lawrence R. Boies, Minneapolis; Louis H. Clerf, Philadelphia; Kenneth M. Day, Pittsburgh; Thomas C. Galloway, Chicago; James H. Maxwell, Ann Arbor; Arthur W. Proetz, St. Louis; and Harry P. Schenck, Philadelphia. Among the outstanding ophthalmologists who will lecture are Drs. S. Judd Beach, Portland, Me.; William L. Benedict, Rochester, Minn.; Daniel B. Kirby, New York; Peter C. Kronfeld, Chicago; and Donrmann K. Pischel, San Francisco.

The Midwinter Seminar follows immediately the Pan-American Congress of Ophthalmology, which will be held in Havana, Cuba, January 5-10, 1948. The dates chosen for the two meetings make possible a delightful opportunity to attend both and at the same time enjoy a winter vacation amid unsurpassed resort attractions.

#### MICHIGAN POSTGRADUATE CLINICAL INSTITUTE

The Second Annual Michigan Postgraduate Clinical Institute will be held at the Book-Cadillac Hotel, March 10-12, 1948. Forty-nine outstanding clinicians and lecturers will present a concentrated three-day postgraduate course covering the newest developments in medicine, surgery, obstetrics, pediatrics, dermatology, ophth-otolaryngology and general practice.

Two evening sessions will be held, the Wednesday night presentation being a "question box" and the Thursday evening program being a panel discussion on "First Aid to the Acutely Injured Patient".

All members of the American Medical Association and of the Canadian Medical Association are cordially invited to attend. There will be no registration fee.

#### SOUTHEASTERN SURGICAL CONGRESS

The Sixteenth Annual Assembly of The Southeastern Surgical Congress will be held in Hollywood, Florida, Hollywood Beach Hotel, April 5-8, 1948. Included in the list of men who will appear on the program are the following members of the Louisiana State Medical Society: Drs. F. F. Boyce, W. E. Kittredge and Ambrose Storck; all of New Orleans.

#### SOCIETY FOR THE PREVENTION OF ASPHYXIAL DEATH, INC.

For many years Dr. Chevalier Jackson has urged that all physicians become familiar with the "death zone of the respiratory tract." For the last fifteen years the Society for the Prevention of Asphyxial Death, Inc. has labored to make the physician "asphyxia conscious." Since April of this year, classes in laryngoscopy and intubation have been given at the Manhattan General Hospital in co-

operation with the S.P.A.D., Inc. Other courses are planned for the New York Eye and Ear Infirmary.

Wide spread interest in these courses, approved by the Council on Medical Education and Hospitals of the American Medical Association, is suggested by the enrolment of physicians in the following specialties who have taken this course—Anesthesia, Eye, Ear, Nose and Throat, Internal Medicine, Industrial Medicine, Obstetrics, Gynecology, Pneumatology, Pediatrics, Plastic Surgery, Oral Surgery, Chest Surgery, General Surgery. These physicians came from Canada, Colorado, Connecticut, Florida, Iowa, Indiana, Illinois, Maryland, Massachusetts, Michigan, New York, New Jersey, Nebraska, Ohio, Pennsylvania and Virginia.

The course stresses the stages of asphyxia, the pathologic physiology of each stage and the indications for treatment. Resuscitation apparatus and resuscitation gadgets are considered important only in so far as they meet the pathologic indication for treatment.

The purpose of the course is clear cut. It is to save lives now lost during anesthesia and other forms of acute asphyxial accidents. Classes are limited to 12 students. A course will be given December 5-6 and January 2-3 in New York City; January 14-15 in Los Angeles; January 21-22 in Honolulu, Hawaii; February 6-7, March 5-6 and April 2-3 in New York City. For further information address: Pneumatology; Manhattan General Hospital, 307 2nd Avenue, New York City.

#### THE EYE-BANK FOR SIGHT RESTORATION, INC.

Fellowships for research in ophthalmology have been granted to the medical schools of Harvard and Yale Universities by The Eye-Bank for Sight Restoration, Inc., it has been announced by Mrs. Aida de Acosta Breckinridge, Executive Director.

Recipients of fellowships will devote themselves chiefly to problems related to the cornea. It is expected that the knowledge thus acquired will aid in the conservation of vision and the restoration of sight among thousands of individuals. One of the principal objectives of research carried on at the present time is the discovery of a method for the preservation of corneal tissue for a period longer than 72 hours.

The Eye-Bank for Sight Restoration, Inc., collects healthy corneal tissue from human eyes for transplanting to blind persons who have lost their sight because of corneal defects. Its national headquarters are located at 210 East 64th Street, New York City, where it maintains its own research laboratory.

The operation substituting a healthy cornea for a damaged one can restore sight in only one type of blindness—that caused solely by opacity of the



cornea when the rest of the eye and optic nerve are normal.

#### FELLOWSHIPS FOR POSTGRADUATE STUDY

The National Jewish Hospital at Denver announces a program of Fellowships for postgraduate study in tuberculosis and allied diseases. Fellows will be appointed for three-month, six-month or one year periods. Further information can be obtained by communicating with Dr. Edgar Mayer, Chairman, National Medical Advisory Board, National Jewish Hospital at Denver, 470 Park Avenue, New York or to Dr. Allan Hurst, Medical Director National Jewish Hospital at Denver, 3800 East Colfax Avenue, Denver.

#### INSTITUTUM DIVI THOMAS

Importance of clinical medicine in scientific research is emphasized by the Institutum Divi Thomas, Cincinnati, O., graduate research institution, in its recent appointment of a Clinical Advisory Committee.

Nine outstanding physicians and scientists from various parts of the United States have been appointed to the Clinical Advisory Committee, according to an announcement by Monsignor Cletus A. Miller and Dr. George S. Sperti, president and director respectively, of the Institutum Divi Thomas.

This committee will serve in a consultant capacity to the Institutum in the clinical aspects of research, carried on in laboratories of the Institutum and its 13 affiliated units.

The Institutum Divi Thomas, founded in 1935 by the Catholic Archbishop of Cincinnati and Dr. Sperti, is devoted to fundamental scientific research. Its scientific activities, at the graduate level, are carried on in the Institutum laboratories in Cincinnati and Palm Beach, and at 13 laboratories in various parts of the United States which are affiliated with the Institutum's research program.

There is an affiliated unit at St. Mary's Dominican College, New Orleans.

#### HEALTH IN NEW ORLEANS

The Bureau of the Census, Department of Commerce, from the figures secured from the New Orleans Health Department, reported that during the week which ended October 11, 137 persons died in the City of New Orleans. Of these 76 were white individuals, 61 nonwhite and eight were children less than one year of age. The next week, ending October 18, showed an increase in number of deaths, there being 179 reported this week. One hundred and fourteen of these deaths occurred in the white population and 65 in the colored. Twenty-six deaths occurred in infants this week, divided 12 and 14 between the white and colored races, re-

spectively. There was a decrease of 47 in the number of deaths reported for the week which came to a close on October 25. Eighty-eight white persons died this week and 44 deaths were reported in the nonwhite population. Death of 11 white infants and six colored children was reported during this particular week. There was only one more death reported during the week which terminated November 1, over the number reported the preceding week. These were divided 81 white, 52 nonwhite and 12 infant deaths; divided equally between the two races.

#### INFECTIOUS DISEASES IN LOUISIANA

The weekly morbidity report for the State of Louisiana for the week ending September 27 indicated that cancer and pulmonary tuberculosis were still the most prevalent reported diseases occurring in the state. There were 37 cases of cancer reported and 35 of pulmonary tuberculosis. These were the only two diseases reported in numbers greater than ten. Undulant fever occurred in two parishes; Lafourche and Washington Parishes each reported one case. There was one case of meningococcus meningitis reported in Jackson Parish and one case of poliomyelitis in East Baton Rouge. The following week, ending October 4, the report showed cancer still at the top of the list with 45 cases, followed by 28 cases of pulmonary tuberculosis, 16 of unclassified pneumonia and 11 of whooping cough. Two cases of malaria were reported and it was stated that both of these were contracted outside of Continental United States. There were no poliomyelitis cases reported this particular week, however one case of meningococcus meningitis was reported in Rapides Parish and two cases of undulant fever were reported in Washington Parish. Measles led all reported diseases on the list for the week ending October 11. There were 49 cases of this disease reported followed by 26 of cancer, 23 of pulmonary tuberculosis and 11 of unclassified pneumonia. Again there were no cases of poliomyelitis reported. One case of meningococcus meningitis was reported from Ascension Parish. There were 50 cases of pulmonary tuberculosis reported for the week which terminated October 18, followed in order of frequency by cancer with 20 cases, unclassified pneumonia with 16 and hookworm infestation with 11. One case of poliomyelitis occurred in Orleans Parish and no cases of meningococcus meningitis were reported this week. Cancer was again at the top of the list, with 47 cases reported the week ending October 25. Pulmonary tuberculosis closely followed with 44 cases and then unclassified pneumonia with 13; these being the only diseases listed in numbers greater than ten. Two cases of poliomyelitis were reported this week; one from Morehouse Parish and one from Orleans. The same order of frequency of cases of cancer, pulmonary tuberculosis and unclassified pneumonia

occurred during the week which ended November 1, these being as follows: cancer 52, pulmonary tuberculosis 50 and unclassified pneumonia 36. One case of meningococcus meningitis was reported from St. Bernard Parish and two cases of poliomyelitis, one each from East Baton Rouge and Livingston Parishes.

MONTHLY MORBIDITY FOR  
VENEREAL DISEASES  
STATE OF LOUISIANA

Month Ending September 30, 1947

	Total This Month	Total Previous Months	Total To Date 1947
CHANCROID .....	53	433	486
GONORRHEA .....	1101	10040	11141
GRANULOMA INGUINALE .....	11	141	152
LYMPHOPATHIA VENEREUM .....	9	62	71
SYPHILIS .....	776	7679	8455

HARRY JOHNSTON  
1870-1947

Dr. Harry Johnston, of Baton Rouge, died on September 26. He had been an active member of the State Society and the East Baton Rouge Parish Society for many years and will be greatly missed by members of the medical profession. Dr. Johnston graduated from the Tulane University School of Medicine in 1900.

LIONEL O. WAGUESPACK  
1878-1947

Dr. Lionel O. Waguespack, of Vacherie, an active and interested member of the Second District and State Medical Societies, died at his home on November 3, 1947. Dr. Waguespack practiced medicine in Louisiana for many years, having graduated from Tulane in 1900.

THOMAS E. WILLIAMS  
1873-1947

Dr. Thomas E. Williams, a member of the Shreveport and State Societies since 1918, died on October 4. Dr. Williams graduated from the Jefferson Medical College in Philadelphia in 1905 and spent most of his years of medical practice in Louisiana.

COMMUNICATION

The Editor,  
New Orleans Medical and Surgical Journal,  
1430 Tulane Avenue,  
New Orleans 13, La.

Dear Sir:

I have been requested by the Board of Administrators of Charity Hospital of Louisiana at New Orleans to clarify the remarks concerning the use of endotracheal anesthesia for teaching purposes in my recent article on "Thiouracil in Toxic Thyroid Disease: Its Preoperative Use in a Public Hospital in a Non-endemic Area," read before the Orleans Parish Medical Society April 14, 1947, and published in the New Orleans Medical and Surgical Journal for August, 1947.

No statement in this article is intended to imply that any method of anesthesia was used in any case in the reported series without the consent and approval of the operating surgeon, on the ground that it was for the interests of the patient that this type of anesthesia should be used. Nor should any statement in the article be construed to mean that the teaching of anesthesia ever superceded the interests of the patient, although the administration of endotracheal anesthesia was taught incidentally in many cases in the series.

These considerations, it seems to me, are self-evident. There is universal agreement that the expert medical care of patients and the education of physicians along special lines not only are not incompatible but actually complement each other. There is also universal agreement that patients cared for in teaching hospitals—which Charity Hospital is accredited as—and used for teaching purposes receive medical care of the highest quality because they are supervised with particular care.

Although, as I have said, these facts are to me so self-evident that they need no elaboration, questions have apparently arisen concerning the statement in my article dealing with the teaching of anesthesia in the New Orleans Charity Hospital. Certainly this statement was not intended to impugn the motives or the judgment of any surgeon who employed it (I happen to use it very frequently myself) nor was it intended in any way to reflect upon the Department of Anesthesia of the Hospital.

I shall appreciate the publication of this note.  
Very truly yours,  
Frederick F. Boyce, M. D.

WOMAN'S AUXILIARY, LOUISIANA STATE  
MEDICAL SOCIETY

The Louisiana State Medical Society has adopted as a postwar activity "Extension of Medical Services through the Louisiana Physicians Service, Inc." We, as members of the Woman's Auxiliary to the Louisiana State Medical Society, are vitally



interested in our own plan. Results are what we are interested in primarily; results not of today, but tomorrow and tomorrow's tomorrow. To achieve these results we must have sound planning and a thorough knowledge of our aims and policies. We must not expect overnight results in our public relations activities, but we must have patience and keep on working. By repetition facts will be stamped on the minds of the public.

First, we must educate ourselves. Begin this study in your own home by informing yourself; learn to know your subject matter so well you can discuss it with confidence and at ease on any occasion. Discussing current medical problems at home will serve two purposes. It will develop your ability to talk convincingly to the public, and it will contribute to your husband's knowledge of what is being done along these lines. Your next step is to coordinate your knowledge with that of other auxiliary members at your regular meetings.

There are many proposed bills before our National Congress today. Among them is the Truman Health Bill. The Murray-Wagner-Dingell Bill is expected back in a new frock. We know the aim of the medical profession is to put good medicine within the reach of all people. We should let others know of this undertaking. Any medical care plan must be organized on a scientific basis and operated under medical supervision. It is no longer a question of a change in medicine; the change is before us. It is now a question of who will shape the operation of the plan. We must not fail!

Many states are finding prepayment medical plans very successful. However, all these projects need publicity and the public must be adequately informed. The medical profession has demonstrated its ability to do a good job by the high quality of its service to mankind. The government should not be allowed to usurp the administration of medical care. The public is beginning to comprehend! It is alert, and as auxiliary members we must keep informed of what prepayment benefits are, and how they can be obtained through Louisiana Physicians Service, Inc. and Blue Cross, stressing always that the private practice of medicine is superior to any government controlled medicine. Create study groups among your auxil-

iary members and educate yourself. That is tremendously important! The American Medical Association is counting heavily on the medical auxiliary in the fields of public education. Our auxiliary is a liaison between the physician and the public. Let us develop a spirit of understanding and friendship between the laity and profession. We quote Dr. Edward Leroy Bortz, President of the American Medical Association, as saying, "The members of the Woman's Auxiliary excel in public relations, and the American Medical Association expects much from you this year in that respect. No group in the nation is so well qualified to speak for social aspects and personal contacts as are the women who know doctors better than anyone else in the world. The Bureau of Health Education is prepared to supply you with any type of material you may need. We recommend in particular the brochure on 'Voluntary health insurance versus compulsory health insurance.' We also recommend that you read 'The Road to Serfdom', published by the University of Chicago Press."

The Woman's Auxiliary to the Shreveport Medical Society on November 12, sponsored an open meeting for the public at the Louisiana State Exhibit Building. Participating in the round-table discussion of state voluntary prepayment medical care plan were Dr. H. Whitney Boggs of Shreveport, Dr. O. B. Owens of Alexandria and Mr. Frank Lais, Jr., of New Orleans.

Mr. Lais spoke on "The Doctor Assumes His Obligations" and explained the organization of the Louisiana Physicians Service and the prepayment surgical and obstetrical care plan. An insurance accountant, Mr. Lais was formerly associated with the Department of Insurance of Louisiana. He became affiliated with the State Medical Society over a year ago and assisted in the organization of the Louisiana Physicians Service. Also, he is executive director of the council on medical service and public relations of the Louisiana State Medical Society.

Every doctor's wife should consider it her personal responsibility to assist in promoting the prepayment medical care plan in her community. The success or failure of these plans may determine whether the medical profession will continue to control the practice of medicine or if it will be taken over by the government.

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## BOOK REVIEWS

*Dermatologic Clues to Internal Disease:* By Howard T. Behrman, M. D. New York, Grune & Stratten, 1947. Pp. 165. Illus. Price, \$5.00.

According to the preface, the author's purpose in presenting this little book is to "correlate the

manifestations of skin disorders with those arising in some visceral dysfunction."

Approximately 160 diseases are discussed alphabetically within 165 pages. Most of these conditions are disturbances of internal function with

either minor or major skin manifestations. Actually, the subject matter is too inclusive for such a small volume. Sample topics are: the avitaminoses, blastomycosis, coronary occlusion, ectopic pregnancy, endocrine disorders, erysipelas, gangosa, gonorrhea, hay fever, influenza, lupus erythematosus and yaws. With 118 black and white illustrations, most of which are good, taking space, there is little room left to do much more than list diseases. For example there are only six lines devoted to the subject of erythema multiforme. Much space is lost by listing the same disease under different names and stating that it is discussed under another heading.

While some readers will be disappointed, whether they be dermatologists or internists, the book does emphasize the fact that skin disturbances are often the reflection of internal disorder.

LEE DAVIDSON MCLEAN, M. D.

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*Surgical Pathology*: By William Boyd, M. D., Dipl. Psychiat., Mr. R. C. P. Edin., F. C. C. P. London, LL. D. Sask., M. D. Oslo, F. R. S. C. 6th ed. Philadelphia, W. B. Saunders Co., 1947. Pp. 858. Illus. pl. Price, \$10.00.

The content and form of the sixth edition of *Boyd's Surgical Pathology* are very much the same as the previous editions. The author presents the pathology in relation to symptomatology and the subject matter is accurate, concise and for the most part complete. The bibliography is excellent and the index adequate. Several additional subjects are discussed such as, tumors of the larynx, avitaminosis, fibrositis of the back, Bittner's milk factor, and the Papanicolaou stain. An interesting addition is the section on congenital heart disease. Everyone is familiar with the author's "easy-to-read" fluid style which is another factor in making this book outstanding. There is a definite improvement in the grade of paper resulting in much better illustrations of the excellent photographs and photomicrographs.

ERNEST G. DEBAKEY, M. D.

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*Hospital Care in the United States*: Prepared by the Commission on Hospital Care, New York, The Commonwealth Fund, 1947. Pp. 631. Charts. Price, \$4.50.

This book is the report of the findings and opinions of the Commission on Hospital Care, an independent public service committee, established by the American Hospital Association and composed of twenty members representing the fields of medicine, dentistry, hospital administration, public health, nursing, education, industry, agriculture and labor. The need for intelligent plan-

ning for the future development of hospital care programs is the main theme of this study. In addition, the necessity for the integration of hospital care with other medical care and social service facilities of the community is clearly indicated.

The report, which deals primarily with general hospitals, presents interesting data concerning the development and growth of hospitals as an institution for medical care. Relationships of hospitals to community life and organizations are also well analyzed. Information will be found in this book which is especially useful to (1) state hospital study groups which have been organized by state governments as the result of the Hospital and Survey Construction Act, Public Law 725, (2) hospital administrators, and (3) others who are interested in the general medical care program of the community. The many functions and services of the general hospital are discussed in detail, and pertinent problems of hospital management, such as size and distribution of hospitals, estimation of bed needs, training of professional personnel, and financing of hospital care, receive adequate attention.

This book is unique in that it sets forth, at the very beginning, a concisely stated summary of the conclusions and recommendations which resulted from the two-year study of the Commission on Hospital Care. Subsequent chapters give full discussions of the factors which led to these opinions reached by the Commission.

KIRK T. MOSLEY, M. D.

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*Stereoscopic Atlas of Neuroanatomy*: By H. S. Rubinstein, M. D., Ph. D. and C. L. Davis, M. D. New York, Grune & Stratton, Inc., 1947. Pp. 19. Illus. pl. 43. Price, \$7.50.

This atlas comprises 43 plates printed individually on cardboard (6 $\frac{7}{8}$  x 9 $\frac{1}{4}$  inches) for convenience of viewing with the stereoscope. Each plate carries a pair of stereoscopic photographs printed in the bottom section, the area above being occupied by a fully labeled line drawing of the specimen. A 19-page booklet accompanies the atlas. It includes a guide for making dissections comparable to those illustrated and a subject index to the structures shown in the plates.

The first five plates in the series are devoted to the embryological history of the brain. The remaining plates illustrate surface features of the brain and gross structures exposed by dissection.

It was an excellent idea that led to the preparation of this atlas, for such a collection of photographs could serve a highly useful purpose. The execution, however, falls short of fulfilling the idea. Too many of the photographs are technically faulty, and in some instances the dissec-



tions themselves do not have the quality to be expected in a work of this kind.

HAROLD CUMMINS, Ph. D.

*A Manual of Fractures and Dislocations:* By Barbara Bartlett Stimson, A. B., M. D., Med. Sc. D., F. A. C. S. Philadelphia, Lee & Febiger, 1947. 2d., Pp. 223. Illus. Price, \$3.25.

In the second edition of "A Manual of Fractures and Dislocations", Dr. Stimson has extensively revised the material presented. This revision is especially noticeable in the discussions of fractures of the humerus and fractures about the elbow. The text is written in a precise, almost cryptic, manner without exhaustive details, but with proper emphasis on both diagnosis and principles of treatment, which enhances its value as a guide for medical students. As a synopsis of fracture treatment, it fulfills its purpose admirably. If any criticism could be made, it would be directed toward the discussion of the time of immobilization of various fractures, which is included in the discussion under each separate fracture. The reviewer feels that there is a distinct probability of the students' getting the impression that a certain type of fracture is treated for such and such a period, and no more or no less. This criticism is extremely minor, considering the overall, thorough discussion of fundamentals of the diagnosis of fractures, bone repair in fractures, and the symptoms and signs of fractures, plus the thorough, if brief, discussion of the principles of treating fractures in general. This valuable guide for medical students should aid them in securing a pathway through the wealth of material published in text books or other larger texts on fractures.

JACK WICKSTROM, M. D.

*Renal Hypertension:* By Eduardo Braun-Menendez, Juan Carlos Fasciolo, Luis F. Leloir, Juan M. Munoz and Alberto C. Taquini. Translated by Lewis Dexter, M. D. Charles C. Thomas, 1946. Pp. 451. Illus. Price \$6.75.

The contributions of the Argentine physiologists under the guidance of Houssay, to the present knowledge of experimental renal hypertension are set forth in this volume. The subject is developed in chronologic order, beginning with studies of the production of the hypertension of renal ischemia and terminating with a description of the

homeostatic influence on blood pressure of the secretions liberated. Complete description of the nature and behavior of renin, hypersensinogen (renin activator) and hypertensin (angiotonin) is given including methods of their preparation.

The book contains a preponderance of the authors' experiments and deals other investigators short in some instances. It obviously will be of more interest to investigators than clinicians. Its large bibliography is helpful to those interested in the subject.

STANLEY COHEN, M. D.

*Care of the Breast:* By Else K. LaRoe, M. D. New York, Froben, 1947. Pp. 240. Illus. Price, \$3.75.

This book is an endeavor by the author, Else K. LaRoe, M. D., to present the subject of the "Care of the Breast" in a lucid and comprehensive manner. The basic consideration is emphasis on certain antecedent pathologic manifestations which so frequently occur in cancer of the mammary gland and other chronic if not fatal, diseases. The embryology, anatomy, anomalies, tumors and reconstructive surgery of the female breast are all covered in this book which contains a total of 76 illustrations and 240 pages. A number of the illustrations are historic in character and a great part of the book is devoted to plastic surgery. Little space is given to radical surgical technic in cancer of the breast.

C. W. JOHNSON, M. D.

*Synopsis of Allergy:* By H. L. Alexander, A. B., M. D. New York, C. V. Mosby Co., 1947. Pp. 255. Price, \$3.50.

The second edition of this compact summary clarifies nicely current ideas in the field of allergy. Much remains to be clarified however in our understanding of the complicated immunologic and physiologic processes that underlie allergy.

The most significant advances since the first edition of this book include the introduction of the antihistaminic drugs, work in vascular allergy, and newer conceptions of the relation of allergy to infectious diseases and of sensitization to drugs and chemicals.

To those desiring a synoptic view of allergy this book can be unreservedly recommended.

V. J. DERBES, M. D.

## PUBLICATIONS RECEIVED

The Blakiston Company, Philadelphia: *History of Medicine* by Cecilia C. Mettler, A. B., Ed. B., A. M., Ph. D.

The C. V. Mosby Company, St. Louis: *The Oculatory Muscles*, by Richard G. Scobee, B. A., M. D.

W. B. Saunders Company, Philadelphia: *Gifford's Textbook of Ophthalmology* (4th edition), by

Francis H. Adler, M. D.; *Pharmacology Therapeutics and Prescription Writing* (5th edition), by Walter Arthur Bastedo, Ph. G., Ph. M. (Hon.), Sc. D. (Hon.), F. A. C. P.; *A Textbook of Clinical Neurology* (6th edition), by Israel S. Wechsler, M. D.

The Williams and Wilkins Company, Baltimore: *An Atlas of Anatomy* (2d edition), by J. C. Boileau Grant, M. C., M. D., Ch. B., F. R. C. S. (Edin.).

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### THE PATHOGENESIS OF THE EDEMA OF CONGESTIVE HEART FAILURE\*

E. H. BRESLER, M. D.

NEW ORLEANS

#### INTRODUCTION

In selecting the topic of this thesis my intention was to choose a commonly encountered clinical phenomenon, yet one concerning which there was some controversy in the literature. In so doing, I hoped to avoid a simple bibliographical survey, allowing myself the privilege of selecting only that portion of the literature which appeared to contribute toward a more rational viewpoint. As a result this thesis is admittedly biased, my only justification in this regard being a deep personal conviction concerning the essential validity of its contents.

The problem of fluid balance and renal function has long attracted my interest. The relation of this problem to that of congestive failure was made clear to me by an article on water and salt balance in congestive failure by Burch and Reaser.<sup>1</sup> My interest was further stimulated by an article on the fluid dynamics in congestive failure by Warren and Stead.<sup>2</sup> It then occurred to me that the problem of the pathogenesis of cardiac edema would be a desirable topic which would afford me the opportunity of familiarizing myself with one of the fron-

tier fields of medicine about which our concepts are undergoing rapid change.

The foregoing thesis makes no pretense at an objective survey of the subject, but is written rather in the spirit of attempting to find an answer to one of the unsolved problems in medicine.

#### EDEMA

Edema is associated with a variety of pathologic conditions, one of the most commonly encountered of which is disease of the heart. It is the purpose of this paper to review the classical mechanisms relating failure of the myocardium with the dropsical state, and to discuss in some detail recent experimental evidence pointing toward a new and entirely different concept.

The term edema is most simply defined as an abnormal collection of fluid in the intercellular spaces. However, such a simple definition does not do justice to the variety of types encountered clinically. It is therefore important to differentiate between two major types of edema, generalized and localized. The distinction was made very clearly by Starling<sup>3</sup> in the eighth of a series of remarkable lectures published in 1912 under the title, "The Fluids of the Body", from which this excerpt is taken: "The term dropsy may be used to denote either an increased amount of fluid in the connective tissue spaces, especially of the skin, when it is sometimes designated as anasarca or oedema, or an accumulation of fluid in the serous spaces of the body, as in conditions of hydrothorax and ascites. In some cases the production of oedema may be brought about by local changes, and therefore in-

\*Awarded the Querens-Rives-Shore Award to the Senior student at Tulane University School of Medicine for the best thesis on cardiology.

volves merely a different distribution of the body fluid. Often however, the increase of fluid in the connective tissue spaces, including the serous spaces, is more or less general and may be associated with a simultaneous increase of the other chief fluid of the body, namely, the blood."

This distinction between the two types of edemas, while seemingly an obvious one, carries with it certain fundamental implications which are pertinent to the ensuing discussion. In considering localized edemas two common examples come immediately to mind, namely those following lymphatic obstruction and those following tissue injury, be it mechanical, thermal, or chemical. If one were to obstruct the lymphatic return in a limb or subject the limb to some type of trauma, edema will appear in this part even though no fluid was ingested by the organism throughout the experiment. Hence such edemas are not concerned with the balance between fluid intake and output. This is in sharp contradistinction to generalized edematous states wherein the total fluid content of the body is increased. Such a state must obviously be dependent upon a disproportion between the fluid intake and output of the organism.

The edema of congestive heart failure is characterized by an increase in the total fluid content of the body, sometimes attaining such proportions that the elastic limit of the confining skin membrane is exceeded and spontaneous rupture takes place. The apparent localization of this edema is an artefact produced by the action of the force of gravity, the greatest accumulations appearing in the most dependent regions of the body. Cardiac edema may be differentiated from the generalized edema of nephrosis and hypoproteinemia by virtue of the fact that together with the increase in interstitial fluid volume there is a simultaneous rise in blood volume as shown by Gibson and Evans,<sup>4</sup> Warren and Stead,<sup>2</sup> Seymour et al.,<sup>5</sup> whereas it has been pointed out by Warren, Merrill, and Stead<sup>6</sup> that blood volumes are essentially normal in the case of edemas associated with low serum proteins. Levine<sup>7</sup> used this feature

to differentiate the edema of nephritis from that of heart failure in a patient. The blood volume in this patient was normal and subsequent studies on the dynamics of the circulation supported the fact that the patient did not have heart failure. Cardiac edema may be differentiated from the edema of acute nephritis due to the fact, as stated by Fishberg,<sup>8</sup> that the protein content of the edema fluid is lower in the former.

The prevailing concepts with regard to the mode of origin of edema, which have been in general acceptance for the past fifty years since Starling's original publication, have been based upon the factors affecting filtration and absorption of fluids at the capillary interface. Attention has been so strongly focused upon the microscopic capillary segment that the relations of fluid balance to the organism as a whole have been neglected. Reasoning from a theoretical consideration of the interplay of the various forces involved in the exchange of fluids across the capillary membrane, it is said that in heart failure, conditions arise which tend to increase the rate of filtration and decrease the rate of reabsorption. This in turn is then said to cause an efflux of fluid from the blood stream into the interstitial spaces resulting in edema. While it cannot be denied that such a shift of fluid might conceivably cause edema, one then wonders why the urinary output is diminished in patients with congestive failure. One might suggest that as a consequence of the fluid efflux the blood becomes concentrated, thus hindering urine formation. However, no such concentration of the blood has been demonstrated. In fact, Seymour et al.,<sup>5</sup> as well as others, have shown that in congestive failure there is a dilution of the blood as evidenced by low serum protein concentrations. This and many other observations cast considerable doubt upon the classical concepts of the mode of formation of generalized edemas, and suggest that a new approach to the problem be sought. However in view of the fact that Starling's concepts of edema formation in cardiac failure are, even now, so universally accepted,



a more critical examination of their validity is warranted.

According to the proponents of this theory, the edema of cardiac failure is due to one or a combination of three factors: (1) increased capillary permeability; (2) increased venous pressure; (3) hypoproteinaemia. Each of these in turn will now be discussed in some detail.

#### INCREASED CAPILLARY PERMEABILITY

It has been suggested, but as yet not proved (Landis<sup>9</sup>) that the prolonged slight anoxemia of cardiac decompensation may increase capillary permeability and be partially responsible for cardiac edema. That the capillaries would be so damaged in congestive failure is subject to grave doubt in view of the fact, as pointed out by Burch and Reaser,<sup>1</sup> that one sees no clinical evidence of edema in many severe anoxic states such as the tetralogy of Fallot or at high altitudes where the degree of anoxia is greater than that seen in congestive failure. Furthermore as pointed out by these authors, the protein content of the edema fluid in cardiac failure has been found to be in the neighborhood of 0.5 per cent, a figure too low to have any appreciable effect upon edema formation.

#### INCREASED VENOUS PRESSURE

The factor which is considered to be by far the most important in the pathogenesis of cardiac edema is the increased transudation of fluids taking place at the capillary interface as a consequence of elevated venous pressure. So much reliance has been placed upon this mechanism that if it can be definitely eliminated as even a contributing factor, the classical theories of cardiac edema formation must of necessity be abandoned.

A clear exposition of the purported role of elevated venous pressure in the genesis of cardiac edema has been advanced by Harrison<sup>10</sup> who states as follows: "As has been discussed, rightsided failure is practically always associated with a rise in the venous pressure. This results in a damming of blood in the capillaries and an eventual increase in the intracapillary pressure. Since there is no compensatory increase in

the effective osmotic pressure of the blood, an increased filtration of water into the tissues will be the result. For a time this may be compensated for by a greater volume of lymph flow from the affected part.

However, as the venous pressure rises further, the faster rate of lymphatic drainage may not be sufficient to compensate for the increased rate of filtration and edema will result. Furthermore, if the venous pressure should rise still further, it will tend to interfere with the emptying of the thoracic duct." Harrison minimized the effects of increased capillary permeability.

This theory, because of its simplicity, is certainly tempting. However, it is based upon the assumption that failure of the right ventricle, in and of itself, will produce an elevated venous pressure. This assumption is not supported by direct experiment. In fact investigations designed to test the validity of this concept of "backward pressure" exerted by the failing myocardium have demonstrated clearly and irrefutably that the generalized increase of venous pressure is not directly caused by the failure of the heart as a pumping mechanism. Starr et al.<sup>11</sup> found that by severely damaging the right ventricle of the heart in dogs in both acute and chronic experiments, more than a minimal rise in venous pressure was never produced. In another series of experiments, Starr<sup>12</sup> found that after death the average pressure in the veins of cardiac patients who died with venous congestion, exceeded that of a series of controls who died without heart disease, by an amount approximately equal to the difference present during life. Since the elevation of venous pressure continues to be present even after the heart has ceased beating, it is quite evident that mechanical failure of the heart could have had no part in its production during life. The author ventures the opinion that the increase in venous pressure may be in large part accounted for by the enormous blood volumes which distended the vascular trees.

Further evidence disputing the role of increased venous pressure in edema forma-

tion was furnished by the experiments of Warren and Stead.<sup>2</sup> These investigators observed that in cardiac patients, in whom failure was precipitated by the administration of liberal salt diets, an accumulation of extracellular fluid, evidenced by an increase in weight, occurs before any increase in venous pressure is demonstrable. Associated with this gain in weight there is a proportionate increase in the blood volume, and only as a later manifestation does the venous pressure become elevated. Reasoning from the results of this and Starr's work, one is impelled to the conclusion that the elevation of venous pressure is determined by the overfilling and distention of the intravascular system with an excessively large blood volume.

There are many other facts which militate strongly against any possible role of venous hypertension in the causation of edema. Burch and Reaser<sup>1</sup> suggested the following objections: Ligation of a large vein, the inferior vena cava, just below the renal veins, will result in venous pressure values of six hundred or more millimeters of water pressure in the tributaries without the development of clinical edema in the areas drained. One might object that such a procedure will not affect renal function or impose an obstruction to the emptying of the large lymphatic trunks. These objections are overruled by the fact that in *concretio cordis* or mediastinal caval obstruction there is often marked venous hypertension for prolonged periods without clinical edema. Smirk<sup>13</sup> pointed out that the increased pressure produced by gravity far exceeds that seen in cardiac failure, so that in the upright position a short person with severe cardiac failure may have a lower venous pressure in the ankles than a tall person without cardiac failure.

These observations lead one to the conclusion that lymphatic reserve must be ample to suffice for even the largest transudations resulting from venous obstruction. There are however areas in the body where lymphatic drainage is not so efficient and where even its role in reabsorption is open to question (Peters<sup>14</sup>). These are the peri-

toneal and pleural cavities. Whenever excessive transudation as a result of venous hypertension takes place in these cavities, fluid readily accumulates. This fluid after a time becomes high in protein content assuming the characteristics of the edema of lymphatic obstruction. This would suggest that reabsorption is taking place through the blood capillaries rather than lymphatics. Therefore these transudates are to be considered as special types of localized accumulations of fluid incidental to the venous hypertension, which occurs only after a considerable degree of subcutaneous edema has already accumulated. The behavior of these isolated accumulations of fluid must then be interpreted separately from generalized edema.

#### HYPOPROTEINEMIA

It has been stated by Landis<sup>9</sup> that the general malnutrition due to the decreased appetite and impaired physiology consequent to congestion leads to a state of hypoproteinemia, thereby contributing to the formation of edema in the patient with chronic congestive failure. Seymour et al.<sup>5</sup> found that in a series of 261 cases of congestive failure culled from various sources, the mean plasma protein concentration was 5.67 grams per 100 cubic centimeters. They suggested that such a decrease in serum proteins might be the result of any one or a combination of three factors: (1) inadequate protein intake; (2) excessive protein loss; (3) failure of protein synthesis. The problem was further complicated by the fact that no one had shown whether the decrease in serum proteins was absolute or relative. That is to say, since the plasma volume is greatly expanded in congestive failure, the low plasma concentration of proteins might simply be due to the failure of protein synthesis to keep pace with the expanding fluid volume. That this is exactly the case was indicated in this experiment by virtue of the fact that the total serum proteins was always higher in chronic congestive heart failure during episodes of decompensation than it was during periods of normalcy in any given patient. In view of these revelations, the decreased



serum protein concentration is not seen to occur as a result of the increase in total body fluids. However, it must be noted that once the formation of edema has already proceeded to the point wherein the blood volume is so inflated that the protein deposits can no longer supply it with sufficient serum proteins, then conditions arise which will aggravate the degree of edema already present. The reason for this has been demonstrated by Warren, Merrill, and Stead<sup>6</sup> who found that in the presence of low serum protein values there is a disproportionate increase in the volume of the interstitial fluid compartment as compared to the intravascular fluid compartment. It must be emphasized, therefore that hypoproteinaemia is a result and not a cause of cardiac edema, but that when the latter condition has led to its formation, it may then aggravate this condition.

In way of summary we are now enabled to say that the classical concepts regarding the formation of cardiac edema must be abandoned because: (1) it has been shown that increased capillary permeability probably does not exist in the congestive failure syndrome, and that if it does it cannot conceivably contribute appreciably to the formation of edema; (2) increased venous pressure is the result and not the cause of the plethora and edema which characterize the state of congestive failure; (3) decreased serum protein concentration is the result and not the cause of the accumulation of abnormal amounts of fluid in congestive failure.

It is now apparent that we must abandon the "microscopic capillary segment" viewpoint and consider the organism as a whole, with particular reference to fluid balance, if we are to make any progress in the understanding of the true mechanisms leading to cardiac edema. Let us then begin with certain well known facts concerning water balance: (1) all water which is ingested is absorbed from the alimentary tract; (2) a certain variable, yet relatively constant portion of this is excreted via respiration, perspiration, and defecation; (3) a variable quantity of this water, depending upon the

needs of the organism, is excreted by the kidney.

The kidney then is the organ which is primarily concerned with the maintenance of a normal volume of fluid within the body. Should this organ fail for some reason and the water continue to be ingested at its former rate, then obviously a state of edema will result. This is very nicely illustrated in the case of patients who suffer acute renal shutdown following hemolysis and blockage of renal tubules. Such patients characteristically develop massive edema.

Let us now examine the state of water balance in congestive failure: (1) the generalized edema must result from either an excessive intake or an inadequate output of fluids. Since oliguria and not polydipsia characterizes the state of congestive failure, then failure of kidney function must be at fault; (2) the kidney of congestive failure exhibits no anatomical lesion which could account for this functional failure. Therefore the answer must be sought in some functional aberration or altered physiology of this organ.

The problem now arises as to how we may relate failure of the heart with failure of the kidney. In attempting to determine the precise pathogenesis of this condition, the dictates of logic command that we begin with the primary seat of the disease, namely the heart. Uncompensated myocardial insufficiency may be defined as the failure of the heart, as a pumping mechanism, to maintain a minute output of sufficient volume to supply the demands of the tissues at a given time. Such a state of affairs is intolerable and cannot long be endured. Reasoning along teleological lines one may assume that the organism will react in some manner either to minimize or offset this disturbance. One way by which such compensation could be effected would be an increase of the diastolic filling of the heart which, in accordance with Starling's law of the heart, would enable this organ to contract with greater vigor. This increased diastolic filling could in turn be achieved if the volume of fluid contained in the vascular tree were to be increased.

This precise sequence of events has been beautifully demonstrated in isolated heart-lung preparations by Katz et al.<sup>15</sup> These investigators, working with dogs' hearts found that after a variable period of normal function, the hearts would begin to manifest signs of failure as determined by the decrease in cardiac output and heart's work. In attempting to simulate the conditions of congestive failure, the peripheral resistance was increased in order to maintain a constant arterial pressure (patients with congestive failure characteristically maintain their blood pressure levels). In spite of these efforts, the hearts continued to fail, the venous pressure showing at no time a tendency to rise. If, however, they increased the circulating fluid volume by injecting fluid into the closed conduits of their apparatus, then there was an immediate marked rise in venous pressure leading to an increased diastolic filling of the heart which would then begin to contract with greater vigor as manifested by a rise in cardiac output and heart's work. This state of affairs would persist for a time until the heart's output would again begin to fall. A further increase of circulating fluid volume would then again restore output to its former level. They were thus enabled to maintain a constant cardiac output by successive increments in the volume of fluid until a point was reached where further stretch of the cardiac fibers did not invoke a beat of increased vigor, whereupon the beats became progressively weaker and rapidly ceased.

Although one is not justified in identifying such experiments, in which all of the physiologic variants in the intact organism cannot be simulated, with the sequence of events in congestive failure, one can not deny that these observations are strongly suggestive.

Now let us return to the picture as it presents itself in man. The only way by which blood volume and with it interstitial fluid volume can be increased is, as indicated earlier in this paper, by means of decreased renal output in face of a normal fluid consumption. This we know is precisely what

takes place in the edema-accumulatory phase of congestive failure. In order that an anatomically intact kidney form less urine, one or both of two things must happen: (1) less blood must be delivered to the kidney; (2) more tubular reabsorption of water must take place.

Merrill<sup>16</sup> conducted an experiment designed to determine what abnormality of kidney function led to the oliguria of congestive heart failure. Following the methods devised by Smith and co-workers, he determined renal blood flow and filtration rate using the p-amino hippuric acid and inulin clearance technics on a series of normotensive cardiac patients without obvious renal disease. Patients were selected who would tend to become edematous at bed rest when mercurial diuretics were withheld so that measurements could be made at a time of increasing decompensation. At the same time as the renal function studies were carried out, the cardiac output was determined by the direct Fick principle, using radio-opaque ureteral catheters passed from the cubital vein to the right atrium under fluoroscopic control, this being the most accurate known method of determining cardiac output. He found that in patients with congestive failure renal blood flow was reduced to one-third to one-fifth of normal. The filtration rates were from one-half to one-third normal, giving filtration fractions from 30 to 50 per cent as contrasted with normal values of 20 per cent. It was further found that renal blood flow was reduced to about one-fifth normal when cardiac output was approximately one-half normal, indicating a specific diversion of blood away from the kidney. In the whole series there was a high degree of correlation between the cardiac index (cardiac output per square meter of body surface area) and renal blood flow. This experiment demonstrates in a most straightforward and unequivocal manner that the decreased urinary output in congestive failure is correlated with and dependent upon a reduced cardiac output. Proponents of the "backward theory" of failure might raise the objection at this point that the reduced renal



blood flow might have resulted from the high venous pressure causing congestion in swollen kidneys contained in a tight capsule. This objection was very clearly overruled by the investigator with several patients in whom venous pressure was reduced to normal with mercurial diuretics and kept at a normal value for several days. The renal blood flow still persisted at its low values, demonstrating that venous congestion did not cause this reduction. One of the most interesting facts demonstrated in this experiment is that whereas in this series of patients the cardiac output was rarely reduced below one-half the normal resting value, the renal blood flow was frequently reduced to approximately one-fifth normal, indicating a specific diversion of blood away from the kidneys, organs which normally receive about 20 per cent of the cardiac output.

Although Merrill did not discuss the problem further, it is of some consequence to relate this specific diversion of the blood from the kidney with known facts concerning renal hemodynamics. The vascular architecture of the kidney differs markedly from that of any other organ in the body because of the fact that blood in its course through this organ must pass through two sets of arterioles and two sets of capillary networks.

The degree of resistance to blood flow through an organ is determined largely by the degree of constriction of its arterioles. If the kidney arterioles were to be constricted to a greater degree than those of other organs in the body, then it is manifestly clear that blood will be proportionately shunted away from the kidney. The question now arises as to why there should be a greater constriction of kidney arterioles, and if so, which set is constricted. Smith<sup>17</sup> answered these questions by demonstrating that the degree of constriction of the efferent arteriole is delicately attuned to variations in renal blood flow. When renal blood flow falls, this arteriole constricts so that intraglomerular pressure, which is related to the relative state of constriction of the afferent and efferent arterioles, is

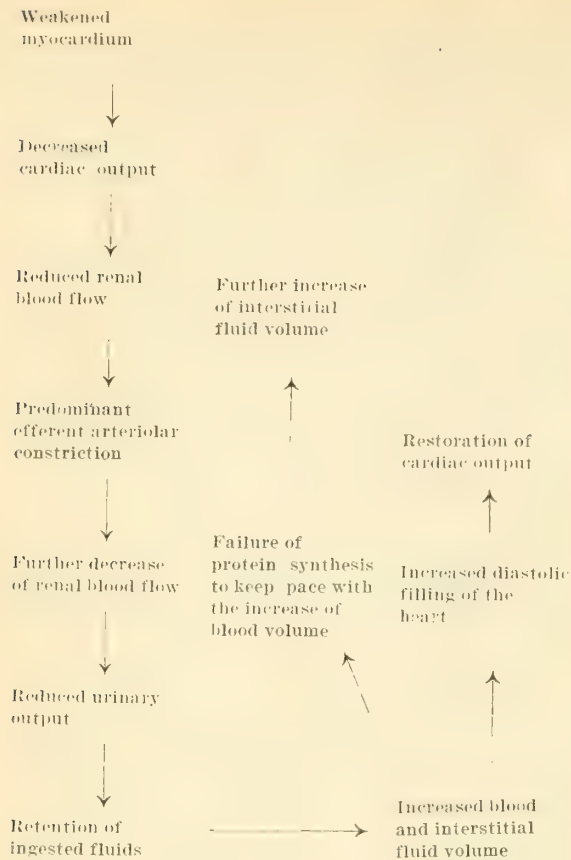
elevated. This independent efferent arteriolar constriction operates so that within wide limits of renal blood flow, a remarkably constant rate of filtration is maintained. Now the higher the intraglomerular pressure, the greater will be the amount of fluid filtered from a unit volume of blood. The percentage of fluid filtered from a unit volume of blood is designated as the filtration fraction and is defined by the ratio: glomerular filtration in c.c. per minute divided by the renal blood flow in c.c. per minute. When this is elevated, it signifies predominant efferent arteriolar constriction. The filtration fractions of the cardiac patients in Merrill's experiment were consistently from one and one-half to two and one-half times the normal values. This then affords the obvious answer for the question why renal blood flow to the kidney was so markedly reduced.

It is of interest to note that Phillips et al.<sup>18</sup> found that a similar diversion of blood flow away from the kidney occurred during experimentally produced hemorrhagic and traumatic shock in dogs. The basic circulatory derangement in both cardiac failure and shock is inadequate output of the heart. In shock it is inadequate venous return which affects cardiac output adversely; in congestive failure it is intrinsic weakness of the myocardium.

On the basis of firm experimental evidence, we are now enabled to trace a remarkable sequence of events whereby urinary flow is diminished in answer to the demands of a weakened myocardium for a greater blood volume with which its diastolic filling will be increased.

The symptomatology of the congestive failure follows logically from such a sequence of events. It has already been mentioned that the increased venous pressure is due to the overfilling and distention of the vascular system. Gibson and Evans<sup>4</sup> lend further support to this with their observation that the average degree of rise in blood volume parallels the average degree of rise in venous pressure in patients with chronic progressive congestive failure.

The reason for the common association



of an abrupt rise in venous pressure and the first signs of clinically apparent edema probably lies in the fact that the elastic limit of the confining skin membrane is being approached. This will be accompanied by an abrupt rise in tissue pressure which will in turn be simultaneously reflected by an upward deflection in the venous pressure.

Although the relationship between a failing myocardium and a weakened vigor of the heart's beat and consequently a drop in cardiac output would seem to be such an obvious sequence of events that the question of its presence would require no defense; such, unfortunately, is not the case. Cardiac output has been investigated extensively by many workers using a variety of technics. The results on the whole have been very contradictory. An exhaustive review of the various procedures with an attempt to evaluate their validity is beyond the scope of this paper. However it is felt

that a discussion of some of the broader aspects of the problem may prove helpful.

Harrison,<sup>10</sup> in an extensive survey of the literature, found that the great majority of investigators agree that the output per minute of the heart is subnormal in patients with cardiac disease. On the other hand "repeated observations on the same individual indicate that clinical improvement with the disappearance of congestive manifestations may be associated with an increase, a decrease, or with no change in the cardiac output per unit of time." This has been considered to be strong evidence against any theory of congestive failure based upon a reduction of cardiac output.

Those who raise these objections must fail to realize that as indicated in the scheme presented above, as soon as there is a momentary fall of cardiac output, compensatory mechanisms go into play to restore volume flow. Hence in a patient with a failing myocardium who is ingesting average quantities of salt and water, blood volume will increase by a given increment with each episode of failure, so that a patient may gradually lapse into a severe congestive state without showing at any given time a significant diminution of cardiac output. With regard to the objection that a given individual in severe failure may have a higher output than at a time when his condition is improved, it must be pointed out that the output of the dyspneic, acutely ill patient in severe congestive failure can by no stretch of the imagination be considered a basal output. No valid conclusions can be drawn from a comparison of outputs which are not strictly basal because exercise alone may drive cardiac outputs to heights tenfold above normal. With these considerations in mind, one must feel that no one can seriously challenge the concept that the cardiac output tends to drop in myocardial insufficiency.

Much attention has been centered in recent years upon the role of the sodium ion in the pathogenesis of cardiac edema. The work of Burch and Reaser,<sup>1</sup> Warren and Stead,<sup>2</sup> Schemm<sup>19</sup> and others has established beyond question the extremely important



part played by the sodium ion in the formation of cardiac edema. No theory regarding the pathogenesis of this condition can be considered either complete or acceptable unless it can account for the edema promoting effect of this ion. One can most logically approach this question by considering what possible effects the sodium ion may have upon the *modus operandi* of the two organs most vitally concerned in the congestive failure syndrome, namely, the heart and kidneys.

Let us begin with a consideration of the heart. It is known from perfusion experiments that the sodium ion is an essential constituent of the perfusate. Hence a deficiency of this ion might conceivably exert a depressant effect upon the myocardium. However, this is of no help because it is the ingestion of salts, not their absence which tends to produce edema. Furthermore no serious chemical imbalance of the composition of body fluids with respect to sodium seems to exist in congestive failure patients. And finally the sodium ion exerts an aggravating effect upon other types of edema which are not associated with cardiac derangement. Hence we may assume with reasonable assurance that the effect of sodium is not mediated through the heart.

Let us now consider the effect upon the sodium ion of function of the kidney. Earlier in this paper it has been shown how this organ is concerned with the maintenance of the volume of body fluids, and it has been indicated that this is controlled by hemodynamic mechanisms regulating the volume of renal blood flow. For the sake of brevity and simplicity, the tacit assumption was made throughout this discussion that the sodium content of ingested fluids was isotonic with the body fluids. However, in reality this is rarely if ever the case, and whenever an imbalance exists the kidney reacts in such a manner that the ionic concentration of the body fluids is maintained at a remarkably constant level. This ability of the kidney to maintain the constancy of the electrolytic pattern of body fluids is primarily the function of the tubules. The precise nature of these processes has been

the subject of intensive investigation, a discussion of which would lead us far afield into the realm of renal physiology. However certain relationships have been clearly demonstrated and are pertinent to this discussion.

When water is taken into the body without sodium, the body fluids are diluted. This presumably prompts the liberation of a hormone which depresses the tubular reabsorption of water. Hence a more dilute urine is excreted until a normal body fluid concentration is attained. On the other hand, when sodium without water is taken into the body, the fluids become concentrated with respect to sodium. This presumably depresses the formation of the diuretic hormone, more water being reabsorbed through the tubule, so that a more concentrated urine is excreted until the normal electrolytic pattern is again attained.

It is then obvious that circumstances will arise in which the kidney, in the defense of the *composition* of body fluids, will have to sacrifice its defense of the *volume* of body fluids; or conversely, it may have to sacrifice composition for volume.

For example, let us consider the case of a patient in progressive congestive failure. If we were to supply this patient water and at the same time withhold sodium, the following sequence of events can be envisioned as taking place: (1) because of decreased renal blood flow due to low cardiac output, this water will tend to be retained leading to a *decreased* urinary excretion; (2) as a result of this retention, the body fluids will be diluted; (3) as a result of this dilution, the tubular reabsorption of water will be repressed leading to *increased* urinary excretion. The net effect upon the volume of urine excreted will then be the resultant of these two opposing mechanisms, the decreased filtration tending to decrease urine volume and the decreased reabsorption tending to increase urine volume. As has been pointed out by Peters,<sup>20</sup> the preservation of normal electrolytic pattern seems to be the most fundamental concern of the kidney. Therefore, in the example cited above, decreased tubular reabsorption will

exert a predominant effect so that any ingested sodium-free water will be promptly excreted. This is in accord with the clinical observations of Schemm<sup>19</sup> who found that on low salts diets patients with chronic congestive failure did not retain water even though they consumed large quantities.

One is then led to suspect that the cardiac patient who is on a normal diet must be consuming a quantity of water which when added to his salt intake will yield a hypotonic solution. He will then excrete that portion of his water intake which is above the amount required to combine isotonicity with his ingested salt. If we now increase his salt intake, he will retain a much greater part of his water intake thereby greatly facilitating the rate of edema formation. That the average diet is in reality hypotonic can easily be seen from the fact that the average sodium ingestion of ten grams when mixed with the average total water intake of two liters yields a 0.5 per cent solution. Because of the fact that a certain proportion of the sodium is obligatorily excreted in combination with acid metabolites, the amount of sodium available for storage in the body fluids is even less than indicated above.

The foregoing explanation for the edema-promoting effect of the sodium ion and the salutary effects which are seen on low salt diets is in complete conformity with the mechanism for cardiac edema proposed in this paper.

#### THERAPEUTIC IMPLICATIONS

Such a radical departure from the conventional concepts regarding the nature of congestive failure as has been set forth in this paper demands a re-evaluation of the therapeutic measures in vogue. Since the accumulation of excess fluid volume is compensatory to the failing heart, the question will be raised as to why such beneficial effects are observed following measures designed to reduce this volume. The answer to this probably is as follows: All patients with chronic congestive failure except in the most extreme terminal stages retain some degree of cardiac reserve. When these patients, in the course of whatever activity

they may participate in become decompensated, they are put to bed. While thus confined, their resting cardiac output can be maintained at a lower blood volume than could the larger output demanded by even moderate activity. Therefore with bed rest alone these patients should begin to lose large quantities of fluid. If one gives digitalis, the heart's action is further improved and an even greater diuresis will result. The action of diuretics is probably simply to catalyze the mobilization of fluids which would take place in time without drugs. It must also be realized that the symptoms of which the cardiac complains most bitterly are those consequent to the plethora and edema which greatly embarrass his respiratory and other physiologic functions. He may feel better in a state of mild shock due to inadequate output than he does with adequate output and severe dyspnea and yet be closer to death. However, dyspnea itself will increase the disproportion between cardiac output and body demands, and should be alleviated as promptly as possible.

One cannot however escape the conclusion that too rigorous salt restriction might deprive an occasional patient of the blood volume he requires, even at resting levels, to prevent him from making a premature exit in shock. One also wonders if the sudden collapse and death of a patient following massive mercurial diuresis might not be explainable upon this same basis.

#### SUMMARY

1. The classical concepts regarding the causation of cardiac edema have been reviewed and found untenable in the light of recent experimental observations.

2. Experimental evidence pointing toward a new concept of the mechanisms involved in the condition have been cited.

3. On the basis of this experimental evidence combined with a teleological approach a hypothesis has been constructed which would appear to explain some of the puzzling aspects of the problem of cardiac edema.

4. Some therapeutic implications of this hypothesis have been discussed.



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## HYPERTROPHIC PYLORIC STENOSIS\*

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Hypertrophic pyloric stenosis is one of the rare anomalies of development of the

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stomach. The condition has its onset between the second and tenth week and is characterized by five major symptoms: (1) vomiting, which is projectile in type and frequently repeated; (2) strong peristaltic waves, plainly visible on the epigastrium, and always moving from left to right; (3) loss of weight, which is often alarming; (4) infrequent and scanty stools, containing mostly mucus and very little fecal matter as seen in "starvation stools", and (5) by a hard, oval tumor, representing the hypertrophic pylorus. The tumor cannot always be palpated and is frequently missed.

## PATHOGENESIS

The pathogenesis of this condition continues to be a subject of dispute. Some physicians feel that the condition is due to spasm of the circular fibers of the pylorus which leads to hypertrophy due to the increased muscular activity, while others hold to the theory of a primary or congenital hypertrophy with a superimposed spasm. The latter theory has the greatest number of adherents. The pathology consists of hyperplasia and hypertrophy of the circular muscle of the pylorus. The pylorus is "olive-shaped", and twice the size of a normal pylorus and is sharply demarcated from the rest of the stomach and duodenum and is nearly as firm as cartilage. The stomach is usually, but not always dilated, and the muscular wall is thickened, especially at the pyloric end.

## CLINICAL PICTURE

The clinical picture is dominated by the five major symptoms as mentioned previously. Vomiting is the initial symptom. It usually starts gradually between the second and tenth week and becomes progressively more severe and constant. Very soon every feeding is vomited and quite frequently a feeding is vomited before it is finished. Vomiting interferes with the infant's nutrition and is followed by a severe loss in weight, amounting to several ounces a day. The character of the stools changes as the amount of food reaching the intestines becomes smaller; finally, the starvation stools contain mostly mucus and very little fecal matter. Peristaltic waves travel-

ing left to right on the epigastrium can be seen in all cases and are most pronounced while or just after the baby has taken a bottle. With the baby placed between the examiner and the light, there appears a mound-like prominence medial to the left costal arch which travels toward the right. Then follows a succession of such prominences separated by depressions or troughs, moving slowly toward the right and disappearing under the right costal arch. There are remissions in the peristaltic waves—then suddenly they will reappear, and when they are most active, the infant will be in evident distress and will squirm and cry and frequently vomit projectily.

The pyloric tumor can at times be palpated, but is more often not palpable.

Simple pylorospasm may be confused with hypertrophic pyloric stenosis, but in these cases it is less severe. The vomiting is milder—there is no loss in weight, but usually a slow, steady gain and the stools are not starvation in type, in that they contain very little mucus.

Due to the persistent vomiting with the loss of acid, there is at times an alkalosis present and in patients who do not go to operation relatively soon, there exist shallow respirations with a diminishing rate to as low as six to eight per minute with well marked periods of apnea.

The roentgen findings in congenital pyloric stenosis are of great value and are usually decisive.

#### TECHNIC

A small catheter is passed into the stomach through the nares if not too narrow, but if they are too narrow, the baby will swallow the catheter easily because it is always hungry. The catheter is followed with the fluoroscope to be sure it does not enter the lungs. If there is a great deal of air in the stomach, some of it may be withdrawn. This accomplished, place two ounces or 60 c.c. of barium mixture into the stomach with a large syringe or by gravity. Films are made in the supine and prone positions every two hours for six to eight hours. If the stomach is not empty,

another film is made in 20 to 24 hours the next morning, and barium will usually be present in the stomach if there is stenosis. The important roentgen signs of pyloric stenosis are elongation of the pyloric canal, delay in or failure of opening of the pylorus, prolonged gastric emptying time, and gastric dilatation with or without excessive peristaltic activity. The base of the duodenal bulb is usually indented. The most informative film to show hypertrophy of gastric musculature is obtained with the patient in the supine position with the left side slightly raised. If there is gas in the transverse colon, the thickness of the gastric wall can be fairly accurately measured from the thin line of the transverse colon to the barium line in the stomach. If the soft tissue shadow measures 4 mm., then hypertrophy should be considered likely, and if over 5 mm., it is certain. In this position the mass may also be felt by the roentgenologist. A large gas filled stomach with very little gas beyond the stomach is also helpful in making the diagnosis. Pylorospasm and hypertrophic pyloric stenosis are differentiated chiefly by the presence of a mass and by the more constant and more marked clinical manifestations, and roentgen signs of obstruction in the latter.

The care of an infant with hypertrophic pyloric stenosis presents a problem that requires careful and adequate therapy directed both by the pediatrician and attending surgeon. Immediate hospitalization is mandatory for this regime in order that careful appraisals of the results of the treatment may be made. In those infants who present a picture of still a fair to good state of nutrition and hydration and who have shown evidences of the disease for only a short time non-operative therapy is the procedure of choice as long as the patient improves and shows no signs of increasing symptomatology. This type of treatment consists of antispasmodics, thick feedings and sedatives with fluids supplemented as required. We believe and are convinced from the care of these patients on our service that any infant who shows extreme de-



hydration, a progression of the symptoms, a continued weight loss or who in any respect fails to respond within 24 to 48 hours of non-operative treatment should be operated upon. In addition, we believe that any infant with this condition who shows signs and symptoms that are severe on admission or any patient whom the history shows to have had the disease over a period of say one week or more should be operated upon.

We consider each of these cases an emergency and once the diagnosis is established all the patients are considered potential candidates for operation and they are immediately treated with that idea in view. As we see more of these patients and the excellent results from operation, we believe less and less in the non-operative treatment and are now proceeding almost entirely with surgical therapy. As soon as the diagnosis is confirmed, these patients are operated upon, the only preoperative requirement being that the infant be in a state of normal hydration, the red cell and hemoglobin be in normal range and the general condition of the patient be such that an operation can be done with a good chance of survival. It cannot be too strongly emphasized that the preoperative care of these infants is the determining factor in their postoperative recovery.

#### COMPLICATIONS

The surgical procedure is the now recognized and established Fredet-Rammstedt operation which is a standardized procedure and differs only very little in its routine applications. We use routinely local anesthesia supplemented by some type of mild preoperative sedation, believing that general anesthesia increases the mortality and postoperative complications. Both the transverse and right rectus incisions have been employed and we prefer the right rectus. The transverse incision does, however, have the advantage of better exposure in those cases in which the pylorus is hard to deliver because of its short attachments and reduced mobility. The only complications of importance during the operation are perforation of the mucosa and hemor-

rhage. Perforation occurred twice in our series, once on the duodenal and once on the gastric side. The rent can be closed by suture followed by omental grafts or suturing of the omentum over the perforation or a second parallel incision may be made through the muscle and the tissue shifted over to cover the rent, it being held in place with sutures. Hemorrhage is at times annoying and originates from the small vessels in the pyloric area. It can be controlled by ligatures or sutures or at times by simple pressure. More recently we have employed the use of thrombin topically in these cases and have found it to be a rapid and simple means of controlling this annoying difficulty. These patients are given fluids by mouth beginning about four to six hours post-operatively and gradually returned to their normal feedings. Supplementary fluids are usually given subcutaneously as required.

#### CONCLUSION

Under this plan of treatment, we (H. H. Hardy) have operated upon 18 of these patients and all have recovered normally. There have been no postoperative complications in the series and no deaths.

#### DISCUSSION

Dr. H. A. White (Alexandria): I have enjoyed Dr. Barker's paper very much; it's a very excellent paper, and, as he told you, I had something to do with writing it.

I would like to stress one point: The collaboration between the surgeon and the pediatrician, or the physician, in these cases. I think our success in Alexandria has been due to the fact we have not let these patients go too far with pyloric stenosis before they were operated upon.

If they become moribund or are almost moribund, then your risk of saving a patient's life is very much greater.

I would like to stress as cardinal signs those that Dr. Barker mentioned, because they are very important, and in that lies your diagnosis. The projectile vomiting is the most frequent. The peristaltic waves, which always pass from left to right; you can see three mounds, and two depressions between those mounds are moving from left to right. The palpable pyloric tumor is present. I must admit, maybe my fingers are not acute enough, but I have never felt one. When it is attached very deep, the pyloric incision is quite difficult to palpate, although it looks like it can be palpated.

Some babies rock along three or four days; if they do not gain and all these symptoms begin,

then that more or less is in keeping with the diagnosis.

Constipation, as he mentioned, is always present, going into, after a few days, what we call a constipated stool. There is another symptom he did not mention, which is abdomen pain. I think these infants have pain, particularly after taking the bottle. They are very irritable and cry a lot. I believe there is very definite pain.

There is a question of the pathogenesis of this situation. I think it is a congenital anomaly: a hypertrophy of the pylorus and followed by the spasms of the muscles which occur, as he told you, around two to six weeks.

We had one case some years ago in a newborn. It was very definite from the start. The child vomited immediately, as soon as they began to feed it. There was constipation; there was subjective vomiting, abdominal pain. We operated on this child on the sixth day, with a typical pyloric stenosis, and the child had an uneventful recovery.

We had another case some years ago that was very interesting, in that it had two situations existing: a stenosis of the esophagus of the cardiac portion and also the pylorus. It happened not to be a hypertrophic affair. I would like to read you the x-ray report we had on that, at this time:

"The lower end of the esophagus shows a stenosis with dilatation above and retention of barium in the dilatation. The barium, however, passes into the stomach, which is filled with gas and after rotating the patient to the right, the barium passes into the duodenum which also shows a restriction, or stenosis. In three hours considerable barium had emptied out of the stomach. A 24 hour film shows a faint outline of the dilated esophagus with constricted cardiac portion and also constriction in the pylorus ring. There is a slight 24 hour retention in the stomach but much less gas as a stomach tube had been used. The barium had passed to the sigmoid. An examination later in the afternoon of the same day showed the stomach empty and the barium in the rectum. An enema resulted in the evacuation of some of the barium.

"The impression was congenital stenosis of the esophagus and the pylorus.

"A recheck of this infant six days later—recheck of the stomach shows a constriction at the lower end of the esophagus with accumulation of barium in the esophagus. However, the barium passes more rapidly than on the previous film. The barium also passes somewhat more rapidly through the pylorus."

This infant had probably more of a spasm than it had a stenosis; even probably more than a stenotic condition of the pylorus. We were successful in passing a small tube into the stomach and, as I remember, we increased the size. Without it,

it was a question of passing it through an opening somewhat restricted. The child made an uneventful recovery in 20 days. There was vomiting, but not the projectile type: his stomach would fill up and he would spit it right back, immediately. And he kept on like that.

So, this is a case where we had two anomalies which, incidentally, turned out very well. This child now, by the way, is 15 years old and doing very nicely.

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## THE TREATMENT OF CHRONIC ANEMIA\*

NORTON W. VOORHIES, M. D.

NEW ORLEANS

An anemia is an abnormal clinical state, which can be treated successfully only by a thorough understanding of its cause. The causes of this condition are numerous, and oftentimes can be determined only by considerable clinical and laboratory study.

The presence of an anemia requires, as do all other medical conditions, a careful history and physical examination. The history of jaundice in the family, or of bleeding from the gastrointestinal tract in a patient, naturally helps to orientate the examiner's thinking and leads to a correct diagnosis. The physical signs of an enlarged liver or spleen, or the presence of pallor, or superficial glandular enlargement, likewise aid materially in arriving at a correct conclusion even before blood studies have been completed.

While a simple blood count is often sufficient, it is advisable to have other determinations, such as a hematocrit, mean corpuscular volume, and mean corpuscular hemoglobin concentration. Through the use of the latter procedures, the recognition of various types of anemia, based on cell size and their hemoglobin content, is made easier. Oftentimes, there is a need for gastric analysis, and gastrointestinal x-rays. Bone marrow studies are in many instances invaluable, though they do require the services of someone trained in their interpretation. The icterus index and the fra-

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gility test may be a necessity, and can be done easily in any laboratory. Special procedures, such as tests for sickling and cold hemolysins, require no unusual skill and only ordinary equipment.

Reznikoff,<sup>1</sup> in an article on chronic anemia, submitted the following useful classification based on etiology, which is listed below with minor changes:

- I. Deficient bone marrow function.
  - A. Faulty bone marrow nutrition.
    1. Iron deficiency.
      - a. Chronic blood loss.
      - b. Defective iron ingestion or absorption.
      - c. Pregnancy.
    2. Extrinsic or intrinsic factor deficiency.
    3. Protein deficiency.
    4. Thyroid deficiency.
    5. Copper and other heavy metal deficiencies.
  - B. Depression of bone marrow.
    1. Toxic nephritis.
    2. Chemical (benzol, gold, sulfonamides, arsenic).
    3. Physical (x-ray, radium).
    4. Chronic infection.
    5. Mechanical, such as leukemia, carcinoma, Hodgkin's disease.
    6. Refractory, such as aplastic anemia.
- II. Hemolytic.
  - A. Intrinsic.
    1. Hemolytic spherocytosis.
    2. Sick cell anemia.
    3. Mediterranean anemia.
    4. Paroxysmal nocturnal hemoglobinuria.
    5. March hemoglobinuria.
  - B. Extrinsic.
    1. Malaria.
    2. Hemolytic — Streptococcus and staphylococcus infections.
    3. Sulfonamides.
    4. Lead.
    5. Favism.

#### THE MICROCYTIC ANEMIAS

The iron deficient anemias are characterized by red blood cells which are small and poorly filled with hemoglobin, and thus

produce a microcytic hypochromic anemia. The existence of this type of anemia is quantitatively shown by a low mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration, the latter usually below 30 per cent. The bone marrow is normoblastic.

An iron deficiency anemia is produced by chronic blood loss and defective iron ingestion or absorption, and by pregnancy. Chronic blood loss is the most common cause of anemia and may be due to a host of things, including bleeding hemorrhoids, esophageal varices, polyps in the bladder or colon, a duodenal ulcer, or hookworm infestation. An iron deficient diet will produce an anemia in infants and children. Iron absorption is interfered with in gastrointestinal disorders, such as chronic diarrhea, gastric resection and anastomoses, and diaphragmatic hernia. Murphy and Hay<sup>2</sup> report an incidence of 26.6 per cent of iron deficiency anemia in the latter condition. A microcytic anemia occurs in pregnant women on an iron-deficient diet because of the demands of the growing fetus. In some microcytic anemias there is a combination of factors, for example, blood loss through menstruation and a deficient diet, as in chlorosis; chronic blood loss, iron deficient diet, and familial predisposition, as in idiopathic hypochromic anemia of middle aged women.

The symptoms of anemia are many. The symptoms common to all types are weakness, palpitation, and rapid pulse. When anemia is severe, ankle edema may occur. There are symptoms and signs characteristic of certain types of microcytic anemias, for example, sore tongue, achlorhydria, diarrhea, dysphagia, and koilonychia, as seen in idiopathic hypochromic anemia. Of special interest is the fact that 39 per cent of patients with chronic hypochromic anemia have some papillary atrophy of the tongue, but this is usually not so severe as that seen in pernicious anemia.<sup>3</sup> According to Darby,<sup>4</sup> chronic iron deficiency alone can produce glossitis and angular fissures. He reports six cases in which improvement

occurred only after the addition of iron to the diet.

The routine use of preparations containing small amounts of iron, liver extract, and vitamins is to be condemned, as usually no one substance is present in a sufficient quantity to relieve the condition should a deficiency in any one of these substances exist. This practice often results in a therapeutic failure, a loss of time, and an unnecessary expense to the patient.

The treatment of the iron deficient anemias is most satisfactory, and, at times, dramatic. An increase in the percentage of reticulocytes follows the administration of iron, and unlike pernicious anemia, the magnitude of response is related to the amount of hemoglobin. The maximum response usually occurs in five to ten days after the beginning of therapy. According to the studies of Balfour et al.,<sup>5</sup> the mucosa of the intestinal tract will absorb iron only when there is a depletion of iron stores in the body. Iron balance is controlled by absorption rather than excretion, which is negligible. Iron given to an anemia not caused by iron deficiency is without effect.

It is of primary importance that bleeding be stopped whenever possible. This is usually not difficult in patients with hemorrhoids and menstrual disturbances. However, it may be a serious problem in a duodenal ulcer or esophagel varices.

It has been shown that ferrous iron is more completely absorbed than ferric iron. Consequently, the former can be used in smaller dosage with as good a result and with less gastrointestinal irritation. There seems to be no justification for the use of the ferric salts. The ferrous salts used today are: Ferrous sulfate, 15 grains per day; ferrous gluconate, the same dosage; and ferrous carbonate, 12 grains daily. Molybdenized ferrous sulphate has been used in the treatment of iron deficiency anemias. Neary<sup>6</sup> reports a more rapid response in the microcytic hypochromic anemias of pregnancy with this drug than with plain ferrous sulfate. According to his report, gastrointestinal disturbances are less frequent. An effective iron preparation will

increase the hemoglobin 1 to 2 per cent per day and will produce a reticulocyte response. It is best to give iron preparations after a meal, as the drug is better tolerated at this time. It is also advisable to start with a small dose, for example, one 5 grain tablet daily for several days, then two tablets for several days, then finally one after each meal. This method of treatment helps to prevent annoying gastrointestinal symptoms, such as nausea, vague abdominal discomfort, and occasional diarrhea. Iron is so effective by mouth that there is no justification to give it parenterally. Intravenous iron in therapeutic dosage is expensive and painful, and, at times, dangerous. Goetsch, Moore, and Minnich<sup>7</sup> gave large doses intravenously, and though a good therapeutic result was noted, there was a high incidence of toxic reactions, such as nausea, vomiting, abdominal pain, and diarrhea. Since copper is present as a contaminant in most iron preparations, and as it is present in the normal diet, the addition of copper is not necessary in the treatment of the iron deficiency anemias of adults. There are those who believe that the microcytic anemia of infants requires copper. However, this is a controversial point. In addition to iron, an adequate diet is important. The diet should include liver, red meat, and eggs. Supplementary vitamins are not necessary unless a definite deficiency exists.

#### THE MACROCYTIC ANEMIAS

The macrocytic anemias are those anemias which are characterized by an abundance of large cells, macrocytes, which are adequately filled with hemoglobin. In such cases, the mean corpuscular volume and the mean corpuscular hemoglobin are increased. The mean corpuscular hemoglobin concentration is usually not altered. The bone marrow is megaloblastic in type. A macrocytic hyperchromic anemia is found in pernicious anemia, and may occur in sprue, tropical and non-tropical, the nutritional anemias, the anemia of pregnancy, and of liver cirrhosis, myxedema, *Diphyllobothrium latum* infes-



tations, and following gastrectomy and intestinal anastomoses. While a macrocytic hyperchromic anemia usually occurs in sprue, there are some cases in which the blood picture is microcytic or normocytic in type. The same applies to idiopathic steatorrhea, or non-tropical sprue, the anemia of pregnancy and of liver cirrhosis. More often than not, a microcytic hypochromic anemia follows gastrectomy and intestinal anastomoses. The pernicious anemia of fish tapeworm infestation is rare. It has been estimated to occur in only 0.1 to 0.2 per cent of persons harboring the parasite. There are those who believe that pernicious anemia in this condition is coincidental. A mild macrocytic anemia occurs in myxedema and seems to respond only to thyroid and not to liver extract.

The macrocytic anemias are treated with some form of liver extract, with the possible exception of that found in myxedema. In pernicious anemia there is an absence of the erythrocyte maturation factor. According to the hypothesis of Castle, the intrinsic factor is not present in the stomach juices to combine with the extrinsic factor in food. Consequently, maturation of the red blood cells is arrested at the megaloblastic stage. Liver and liver extract can be given by mouth, and though effective, are not practicable, as seldom can sufficient quantities be taken orally to restore the blood picture to normal. Liver extract intramuscularly is the route of choice. The average case should be given 15 units daily for one week, and then 15 units twice a week until the red blood cell count and the mean corpuscular volume have reached normal levels. When there are no neurologic complications, injections at two or three week intervals are sufficient, estimating the dose so that the patient will get one unit per day. If neurological complications are present, it is advisable to continue weekly injections of liver extract indefinitely, and to use larger doses than are ordinarily used, that is, 2 c.c. of a concentrate, or a total of 30 units per week. This should be supplemented with oral liver, about a pound per week, as the factor present in

liver, responsible for the improvement of nervous system lesions, is not known, and this factor could have been destroyed in the preparation of a refined product. Adequate liver therapy arrests the progress of nervous system complications, and in 50 to 60 per cent of cases improvement will occur, provided these complications have not been present too long. Lesions of the lateral columns are most resistant to treatment, while posterior columns, peripheral nerve and sphincter control respond more readily.<sup>8</sup> An improvement in general strength and motor performance can be expected. The presence of an infection or of extensive arteriosclerosis renders liver therapy less effective, and should be looked for whenever the response is poor. The error in liver therapy is usually giving too little rather than too much. Large amounts of liver are stored and are not harmful. The patient with pernicious anemia will require treatment for the remainder of his life.

Recent studies with folic acid indicate that a remission can be produced by its use in pernicious anemia, as well as in other macrocytic anemias.<sup>9</sup> While the drug has not yet had sufficient clinical trial, it seems to be capable of relieving many of the symptoms of pernicious anemia, and of restoring the blood picture to normal or near normal levels. However, its ability to maintain a remission is still an uncertainty. So far as is known at the present time, it has not been effective in preventing or relieving the neurologic relapse in some cases of pernicious anemia.<sup>10</sup> Meyer,<sup>11</sup> in a recent report of eleven cases of pernicious anemia and one of sprue, concluded that folic acid, 15-50 milligrams, given orally, or 20 milligrams given intramuscularly, usually produced only a submaximal reticulocytosis, and failed to prevent the progression of neurologic lesions. However, he found that when folic acid was combined with a small dose of liver extract, one-half unit per day, a reticulocyte response occurred which was greater than when adequate amounts of liver were used alone. There was also im-

provement in the symptoms and signs of combined sclerosis in three patients.

In conclusion, it can be said that the treatment of pernicious anemia with folic acid is still in the experimental stage and that it would be unwise to treat a patient with this drug alone over any prolonged period of time.

The patients with pernicious anemia should have an adequate diet, including liver, red meat, and eggs. Sufficient rest and exercise are also important. Dilute hydrochloric acid is only needed when the patient is having gastrointestinal symptoms due to achlorhydria. In such instances, 4 c.c. of dilute hydrochloric acid (USP) in water or fruit juices may be given before meals. Iron is seldom needed in pernicious anemia, unless there has been a recent blood loss. Rarely is the blood picture of pernicious anemia influenced by an iron deficiency. In such cases, the administration of iron is followed by a more characteristic cell appearance.

The anemia of sprue and idiopathic steatorrhea (non-tropical sprue) is thought to be due to absence of extrinsic factor in the diet. While this anemia is usually macrocytic, it may be normocytic or microcytic in type. These cases are greatly benefitted by liver extract, even those with a normocytic or microcytic blood picture, although doses of iron may be needed as well. It is generally conceded that larger doses of liver extract are needed than are used in pernicious anemia, and the results are not nearly as satisfactory.

In sprue and idiopathic steatorrhea careful attention must be given to diet, though the advent of liver therapy has made diet restrictions less rigid. It has been found that these patients do best on a high protein and low carbohydrate and low fat diet. Calcium may be needed as the deficiency is not uncommon, particularly in non-tropical sprue. Additional vitamins may likewise be indicated. Celiac disease, an equivalent of non-tropical sprue, occurring in children, is usually normocytic or microcytic in type, but this likewise is benefitted by liver extract.

Folic acid, parenterally, or given by mouth, has been found to be effective in sprue, both tropical and non-tropical.<sup>9, 16</sup> The symptoms of diarrhea and glossitis are promptly relieved and blood regeneration takes place. The macrocytic hyperchromic anemia of pregnancy, liver cirrhosis, gastrectomy, and intestinal anastomoses responds to injections of liver extract. Folic acid has been used in the pernicious anemia of pregnancy, liver cirrhosis, and nutritional macrocytic anemias with good results.<sup>9</sup> The macrocytic anemia of fish tapeworm infestation responds to injections of liver extract.

As a result of the observations of Lucy Wills in India, macrocytic anemias occurring in natives of the tropics have been recognized. Most of the cases have occurred in pregnant women. However, cases have occurred in non-pregnant women, and in men as well. Many of these patients failed to respond to refined liver extract, but responded to crude forms of the extract. Watson and Castle<sup>12</sup> reported three cases of macrocytic anemia occurring in pregnancy, which responded only to oral liver extract, 1 unit per day, or 15 c.c., t.i.d., of liquid extract of liver (USP Valentine). A fourth case responded only to intravenous liver in large amounts. Apparently, there are macrocytic anemias which are relieved by some unknown substance in liver which is different from the erythrocytic maturation factor effective in pernicious anemia.

Anemia due to an inadequate diet of protein does occur. Whipple's<sup>13</sup> work on dogs has shown that animals depleted of blood plasma will not regain previous hemoglobin levels until protein is restored, despite large amounts of iron. While such an anemia is common, adequate protein intake may be a factor in patients chronically ill, particularly those with disturbances of digestion due to short-circuiting operations on the gastrointestinal tract.

Those anemias which are due to a depression of bone marrow are relieved only by removal of the depressing agent, which in many instances is impossible. The bone marrow, when depressed by chemicals such



as the sulfonamides and gold, or by physical agents such as x-ray and radium, will recover when the depressing agents are withdrawn. Studies by Greenberg et al<sup>14</sup> on patients with infections have shown that iron intravenously fails to produce an increase in hemoglobin. The excess iron is stored in the liver and the hypoferemia persists. The anemia is thought to be due to retardation of hemoglobin synthesis whereby red blood cells break down after their normal life span and replacements are slow in forming. Mechanical interferences with red blood cell formation, such as are found in carcinoma, Hodgins, leukemia, etc., (myelophthisic anemia) can be temporarily relieved with irradiation. The depression of all cellular elements, such as is found in aplastic anemia, is usually a hopeless situation, which can only derive temporary benefit from blood transfusions.

The hemolytic anemias, as shown by the preceding classification, can be grouped into the intrinsic and extrinsic varieties. Congenital hemolytic jaundice is an hereditary disease of blood characterized by red blood cells which have greater thickness than normal cells. These cells are called spherocytes, and according to Haden,<sup>15</sup> are less resistant to hypotonic salt solutions as less swelling can occur before they burst. The illness is characterized by hemolytic crises which result in a tremendous drop in the red blood cell count. Transfusions must be resorted to though reactions are frequent as the donor cells may be hemolyzed. Splenectomy is the procedure of choice and is followed by a relief of the anemia, though spherocytosis continues.

Sickle cell anemia is a blood disorder common to the negro race, characterized by sickle cells, or cells which assume a crescentic shape when exposed to an atmosphere of low oxygen tension. The illness is progressive and fatal, and only temporarily benefitted by blood transfusions. Haden<sup>15</sup> believes that early cases can be improved by splenectomy.

Mediterranean anemia is an hereditary disease of the blood found in people who inhabit the shores of the Mediterranean

Sea, and in the descendents of these people. The disease varies from an individual who is quite normal except for minor blood abnormalities, including an increased resistance of the red blood cells to hypotonic saline solution, to one who has mongoloid facies, a severe anemia, splenomegaly, and bone changes. Target cells may be numerous in this blood disorder. There is no specific treatment. Many cases are mild and need no treatment, while others, the type commonly seen in children, will require the usual palliative measures of blood transfusions, rest, and adequate diet.

Paroxysmal nocturnal hemoglobinuria is a rare type of hemolytic disease in which the hemolysis occurs chiefly at night and seems to be related to a drop in the pH of the blood. The family history is negative. The night urine is dark, while that voided in the day is normal. The fragility test is within normal limits. The outlook is hopeless. Transfusions may be used with temporary benefit, though they are usually attended by severe reactions.

Paroxysmal (cold) hemoglobinuria is a disorder occurring in syphilitics in which exposure to cold causes hemolysis and hemoglobinuria. The anemia is seldom a problem. Treatment for syphilis is often followed by disappearance of the hemolytic reactions.

March hemoglobinuria is not accompanied by anemia. Hemoglobin is found in the urine after a long march or a long distance run. The condition subsides spontaneously with rest.

Those hemolytic anemias which have external causes require the removal of the hemolytic agent for relief. In the case of malaria, atabrine and quinine are used. In streptococcal and staphylococcal infections, penicillin and the sulfonamides are the drugs of choice. Hemolytic anemias which occur in patients during the administration of sulfonamides will usually respond favorably on withdrawal of the drug, though transfusions may be life-saving in the early stages of the illness. Lead anemia is mainly a matter of recognition. The anemia is not severe and is relieved by removal of the

cause. Poisoning with the fava bean may produce a severe hemolytic anemia in sensitive individuals which may result in death. Transfusions as an emergency measure is indicated. An appreciation of the cause and the removal of this agent from the diet is of course a necessity.

#### CONCLUSIONS

Chronic anemias are often a problem in diagnosis and may require all available clinical and laboratory skill to determine the cause.

In some anemias, such as pernicious anemia, sprue, and the iron deficiency anemias, the results of treatment are most gratifying. In others, such as paroxysmal nocturnal hemoglobinuria and sickle cell anemia, there is little to offer the patient except supportive measures. In the anemia of carcinoma, and Hodgkins nothing can be done, as it represents a concomitant of a progressive and fatal illness.

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#### DISCUSSION

Dr. Johan T. Peters (New Orleans): In some of the recent editions of textbooks the blood findings in pernicious anemia are called "macrocytic normochromic", instead of the older term "macrocytic hyperchromic" which is used by the great majority of the hematologists over the whole world. The new term, recommended by Wintrobe, because the mean corpuscular hemoglobin concentration is normal in pernicious anemia, seems to be not only confusing for the students but also wrong. The prefix "hyper means only a larger amount and does not mean a higher concentration of hemoglobin. The old term "hyperchromic" was chosen because in pernicious anemia there is a larger amount of hemoglobin in the red cells, as expressed in the increased mean corpuscular hemoglobin.

Dr. Voorhies (in closing): According to Wintrobe the macrocytic anemias are characterized by the presence of many large cells adequately filled but not overloaded with hemoglobin. Because of the presence of many large cells the amount of circulating hemoglobin is higher than we would ordinarily expect from the degree of anemia present.

As is often demonstrated by pernicious anemia in relapse the high percentage of macrocytes makes life possible in the presence of a severe anemia.

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## RADIATION TREATMENT IN CANCER\*

STAKELY HATCHETTE, M. D.

LAKE CHARLES

The use of x-rays in the field of diagnosis is familiar to everyone, but the uses of x-rays and the gamma rays of radium in the treatment of malignant disease and allied conditions are not so well understood by the average physician and it is the purpose of this paper to try to explain the reasons for using radiation therapy and the results which are obtained.

A brief review of the physical properties of x-rays and gamma rays might be helpful in understanding what they are and how they obtain their effects. Both of these agents are very similar to ordinary visible light in most of their properties and occupy their positions as wave bands in the electro-

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magnetic spectrum just as ordinary visible light rays do. The differences between these rays and light rays with which we, as physicians, are concerned is that they are invisible, are not capable of being perceived by our other senses, are destructive, and cannot be deflected.

The electro-magnetic spectrum is composed of a number of different bands of wave lengths. The longest waves are the wave lengths used for regular radio broadcasting. The next longest group is the band of waves used in short-wave radio broadcasting. This is followed by the band of infra-red rays which has medical uses and with which you are all familiar. Shorter than these, and forming a very narrow band of waves, comes the group of waves forming the visible light spectrum. Then comes the relatively broad group of ultra-violet rays which is the first form of light (or wave groups) capable of causing injury to living tissues by virtue of their powers of penetrating the uppermost layers of tissue and causing injury to the deeper layers. Their penetrating powers are not great, being only sufficient to go one or two millimeters beneath the surface, but each of you who has had a severe sunburn is familiar with the fact that ultra-violet rays can cause damaging effects to the skin. The next shortest group of rays is the band known as Grenz rays. These are more penetrating than ultra-violet rays and have been used most in the treatment of certain skin diseases. These wave-lengths are frequently thought of as the very longest group of x-ray wave lengths and they are usually generated at around 35,000 volts from a tube with a special window to permit the wave-lengths to pass through. Then comes the band of relatively long waves which are used in fluoroscopy and in making of x-ray films. These are followed by the group of even shorter rays used in x-ray therapy and these, in turn, by the gamma rays of radium which are the shortest rays used in medicine. The very shortest group of all is the group known as cosmic rays. Very little is known of them and of their effects so

that they are of no known importance to medicine at this time.

Beginning with the ultra-violet wave band, as the various types of rays become shorter, they become more penetrating. As they become more penetrating, they become more destructive to living tissues. This being true, it may be said that x-rays and gamma rays are forms of light and that they are similar to light in most of their properties, but that they differ from ordinary visible light in that they cannot be perceived by any of the senses and they are destructive to living tissues. These destructive effects cannot be too strongly emphasized and this must be kept constantly in mind in working with these rays, no matter whether they be used in diagnostic procedures or in the administration of treatment. No matter how small the amount of either x-rays or gamma rays be given, and no matter whether they be used for fluoroscopy, the making of films, or the administration of treatment, it must be kept in mind that a certain amount of injury is given to the living tissues, even though it might be infinitesimal, every time they are exposed to the rays. Soon after the discovery of x-rays and radium it was found that both of these agents had a way of causing cumulative effects in the tissues and that repeated short exposures to the rays could cause destruction of living tissues just as effectively as too long a single exposure. This came about, as might be suspected, from the overenthusiastic use of these rays by the pioneer workers in making their fluoroscopic observations, x-ray films, and their administrations of the rays for the purposes of treatment.

From these observations the principle of administering multiple fractional doses of the rays for the purpose of treatment arose.

In studying the effects of radiation upon living tissues it has been found that normal, mature living cells have a greater resistance to the destructive effects of x-rays and gamma rays than do cells which are in the process of division and reproduction, and that the more embryonic the cell types ex-

posed to the effects of the rays the greater are the destructive effects of the irradiation. For this reason, it is helpful to know the degree of embryonicity of the cells in a growth to be treated, and it is because of the fact that these rays are more lethal to cells of an embryonic type than they are to mature cells that the principle of administering them to cancerous growths arose. This fact makes it possible to give a lethal dose of rays to a cancerous growth which is surrounded by normal tissues, yet give a dosage which is short of the amount required to cause destruction of the normal tissues surrounding the growth, and, while it is frequently necessary to give enough radiation to damage the normal surrounding tissues rather severely, it is the object of the radiologist to destroy the abnormal growth but give an amount of radiation insufficient to damage the normal tissues beyond their abilities to recover from the effects of the rays and to heal over the area in which the abnormal growth was present. The normal tissues are practically always irradiated along with the cancerous lesion present within them, or around it, for cancer has a way of invading the lymphatics and blood vessels in its outward extension and these invasions of tissues which seem normal to the unaided eye must be destroyed if it is to be hoped that the patient can be freed of the disease. Not only is it necessary to irradiate the tissues in the immediate vicinity of the new growth, but it is frequently necessary to irradiate tissues some distance away in order to destroy possible extension along the lymphatic drainage tracts and in the regional lymph nodes. This is the reason for giving irradiation over the entire lower abdomen in the treatment of carcinoma of the cervix or body of the uterus; the entire anterior chest wall of the hemithorax and the axillary and supraclavicular areas of the involved side in cancer of the breast, or the submandibular and cervical areas in treatment of cancer of the lower lip.

Because different normal tissues have different degrees of sensitivity to the effects of x-rays and gamma rays, and be-

cause it is sometimes found that it takes a greater amount of irradiation to destroy a new growth than it does some neighboring normal tissue of another type which has to be included in the field of irradiation, it follows that new growths in some areas are best treated by some other type of therapy. For instance, the reproductive portions of the ovaries and testes are very sensitive to the effects of irradiation and are quite easily destroyed, so that irradiation in individuals still in their active sexual lives should be given with extreme care to avoid over-irradiation of these organs, or some other type of treatment may be advised. Lymphatic tissues are next most easily destroyed so that it may be advisable under certain conditions to avoid irradiating the spleen. What is true of these two types of tissue holds for all of the other tissues of the body, but not to such great degree, so that there is not so much objection to directing a beam of x-rays or gamma rays through other types of tissues. These different degrees of sensitivity of the tissues should be kept in mind, however, in planning a course of x-ray or radium therapy to be given to a patient.

One other thing to be considered is that for reasons not yet completely understood, cancer of the gastrointestinal tract—other than the mouth and anus—seems to have quite a high resistance to the lethal effects of the rays and it takes about as much radiation to destroy them as it does to destroy the normal intestinal mucosa. Because of this, cancerous growths of the gastrointestinal tract are not treated by irradiation, but must be treated by surgery instead.

Most malignant growths, however, are capable of being treated by x-ray, by radium, or by a combination of the two. Operation is frequently necessary and, in the opinion of many radiologists, is best done *after* a certain amount of irradiation is given. The reason for this feeling is simple and logical. Because malignant growths show a tendency to early extensions into the lymphatics and blood vessels of the involved area the radiologist feels that simple surgical excision of cancerous growths is



not enough and that, in many cases, both irradiation and operation are best used together if the patient is to be given the greatest chance for recovery. For instance, in the treatment of carcinoma of the breast many radiologists believe that if approximately 1000 r of deep x-ray therapy be given to the involved breast and to the regional lymph nodes and the lymphatic and vascular drainage tracts *before* operation, enough irradiation will have been given to inhibit the rapidly growing cells about the edge of the cancer and to render them less likely to survive in the event some became dislodged at operation and be taken into the lymphatic or vascular circulations to metastasize elsewhere, or in case a few cells be left in the operative field to recur at some future time. The dosage suggested above has seemed sufficient to reduce viability of cancer cells yet it is not enough to cause the blood vessels to become congested and thereby cause the surgeon to have a more difficult, more bloody operation than he would have if nothing had been done in the nature of preoperative therapy. This should be followed by a sufficient amount of postoperative irradiation to complete the destruction of any cancer cells that might remain in the operative field and which may have invaded lymphatic and vascular tracts and lymphatic nodes draining the area. Preoperative irradiation in some degree would seem only a reasonable precaution for no matter how gently an operation be performed, there is some degree of trauma in the handling of tissues which is connected with it and which is likely to dislodge cancer cells. Then, too, the sharpest edge of the scalpel is no smoother than the edge of a saw when viewed under the microscope, and the numerous tiny cracks in the edge of the blade are more than capable of picking up small groups of cancer cells which may be transported elsewhere or which may be washed out of a crack into a blood or lymphatic vessel when one of these is cut into by the knife edge. Preoperative irradiation, if given in the suggested amount, will materially lessen the chance of any of these

small groups of cells being able to survive if they be taken to other locations.

Other radiologists believe that a full dosage of irradiation should be given to a patient with cancer of the breast and that it is a wise precaution to have the breast removed after the radiation reaction has completely subsided. This is based on the fact that there are few, if any, radiologists who have not given a cancerous breast all of the irradiation the skin would stand, had a surgeon remove the breast after the reaction had completely subsided, and then had the pathologist to report that, while the original biopsy showed a cancerous lesion to be present, the breast contained nothing suggestive of cancerous tissue following its removal. There are enough breasts, however, which will show a few cancer cells trapped in scar tissue to make most radiologists feel that removal of the breast is necessary in all cases except those in which operation would endanger the patient's life. In cases where only radiation can be given, many will remain clinically free of disease until death comes from some other cause.

In treatment of carcinoma of the cervix of the uterus a course of deep x-ray therapy should be given first and should be administered through multiple ports over the lower abdomen. The reason for beginning the treatment with the deep x-ray therapy is the same as the reason for giving deep x-ray therapy preoperatively to a woman with carcinoma of the breast; that is, to destroy the rapidly growing edges of the malignancy and to kill any groups of cells which may have extended into the lymphatics draining the area. It will be found that the use of the x-ray treatment first will reduce the size of the growth materially and will greatly lessen the possibility of metastases, and will make it far safer to dilate the cervix sufficiently to permit the insertion of the radium applicator. In this connection, the practice of using a Goodell or Wylie type of cervical dilator cannot be too strongly condemned in dealing with a carcinomatous cervix. While they may be entirely satisfactory in dilating a cervix with non-malignant disease, they cause

tearing of the blood vessels and lymphatic channels and the breaking off of numerous small emboli of live cancer cells which may be washed into these two general circulations and which may easily result in metastases elsewhere. The use of a graduated set of dilators such as the Hank type is a far safer procedure, for dilation with this type of instrument is accompanied by far less maceration of tissues, far less tearing of the blood and lymphatic vessels, and is far less likely to result in metastases. After the course of deep x-ray therapy is given, it will sometimes be found that there is no visible or palpable evidence of the cancer remaining in the cervix. In any case, the size of the growth will be found to be arrested or reduced. This is the time for introduction of the radium to obtain the intense local effects of the rays and to destroy any cells of the original lesion which may still remain in the area. The use of these two agents is usually all that is necessary to eradicate the disease if it can be diagnosed in the earlier stages when it may still be classed as curable. If not diagnosed until it has spread beyond the cervix, the patient may still be able to obtain considerable relief and prolongation of life if given deep x-ray therapy and, in a few cases, clinical cures of the disease may be obtained for periods of five years or more. An operation as a means of treatment for carcinoma in this location has been generally discouraging and has been more or less discontinued except for a few localities.

As mentioned above, x-ray should be used first in the treatment of most malignant disease in which irradiation is to be used. The reason for this is simple. The x-ray tube is usually placed at a considerably greater distance from the lesion to be treated than would be the case if radium were used. As a result of this, the softer radiation which emerges from the tube or which may be set up in the filters used is absorbed by the air through which it passes and does not reach the patient in any great amount. This being so, only the more penetrating, hard rays are administered and these pass into the skin and through the

skin to the depth desired to bring about the changes in the lesion being treated. Thus, in the treatment of carcinoma of the uterine cervix, x-radiation is administered through ports over the abdomen and back and passes through the skin to liberate its effects deep in the abdomen at the location of the cervix. Radium could be used similarly if there were enough radium in the hands of the average radiologist to make up a radium bomb of sufficient strength to approximate the amount of time required to administer x-rays, for radium liberates some rays so hard and penetrating that it requires approximately nine inches of lead to stop them. There are relatively few such rays in a beam of gamma rays, however, as compared to the number of longer, less penetrating rays which are present, and very few radiologists have more than a few hundred milligrams of radium to work with so that the average radiologist has to use the radium available to him in the way it will be most effective; that is, he uses the relatively small amount he has at distances varying from contact up to only a few centimeters and must necessarily use the longer rays low penetrability as well as the very short rays of high penetrability in giving his treatment. This being so, the effects obtained are largely localized to the immediate area treated, are greatest on the surface treated, and show a rapid decline in their effects as the distance from the surface increases. For instance; if radium be administered to the skin surface from a distance of 1 centimeter and the effect upon the skin be classed as 100 per cent effective, the decline in its intensity is so rapid that it would be only 25 per cent effective at a distance one centimeter beneath the skin, in the cervix, and at other locations where intense local effects are desired and where it is capable of being applied; but if a lesion has reached any appreciable size it must be treated by x-rays first so that its size may be reduced to the point where radium will be effective and, at the same time, the use of x-rays first does sufficient damage to the growth to render the possibility of metastases less likely in the event



that the tissues will have to be traumatized by dilatation or by surgical excision of a growth.

It is not the intent of this paper to list the various locations upon and within the body where radiation therapy is used effectively, but it is presented in the attempt to explain what radiation does and how it may be useful in the treatment of malignant disease. The conditions mentioned above were selected mainly because of the fact that malignant disease in these locations is so common as to be familiar to all, but what has been said of them applies more or less to the treatment of cancer in whatever location it may be found.

#### CONCLUSION

It is hoped that the explanations given have helped to clarify some of the confusion about the treatment of cancer by means of radiation, that they will explain why x-ray reactions must be expected if adequate treatment be administered, that they will help the physician in deciding what type of treatment should offer best results to his patient in order that there will be less delay between the diagnosis and the beginning of treatment, and that it is often necessary to use more than one form of treatment if the patient is to be given the greatest chance of a cure of the disease.

Dr. Garcia: (New Orleans): I think Dr. Hatchette is to be highly commended for his clarity and his lucidness in giving us an insight into the manner by which radiation becomes effective in the treatment of cancer. I am also impressed by the range of subjects that he covered in such a short time. For instance, he has given us some information about the physics of radiation, about the reactions of living cells to radiation, about the various explanations for such biological effects and about problems involved in the treatment of carcinoma of the cervix and of the breast.

It must be acknowledged that the full benefits of radiation therapy have not been realized, mainly due to the scepticism engendered by lack of knowledge regarding its true scope. The action of radiation is complex and any effort intended to clarify it is praiseworthy. With greater understanding will come greater clinical application. More lives will be saved by taking full advantage of all therapeutic measures useful in controlling cancer. For forty years there has been an intensive campaign of public education emphasizing the need for early diagnosis. This should be continued, and if successful,

perhaps another generation of physicians will see a preponderance of favorable lesions with high rates of cure. But the bulk of the cancer material we see today is advanced, much of it completely hopeless; consequently, we should place great stress on the efficient employment of both surgery and radiation. It seems justifiable to say that considerable improvement over the results currently obtained can be achieved by increased efficiency in the use of recognized methods. I think Dr. Hatchette has been helpful in our progress towards this goal, by showing us how radiation acts.

There is, of course, a great deal of mystery as to why some tumors react well to radiation and others do not. Intensive research is being conducted of the intracellular chemistry of cells exposed to radiation and valuable information has accumulated. For instance, an enzymatic disturbance occurs, which can be detected by suitable analysis after test doses of radiation, and which may prove dependable in predicting the response of individual tumors. From the practical standpoint, however, we need not wait for such refinements, since we know well that radiation can contribute substantially to the salvage in certain forms of cancer. Furthermore, a better understanding of technic has brought standardization comparable to the standardization of surgical procedures for the major forms of cancer. As a consequence, favorable results can be obtained with consistency.

The question of combining surgery and radiation is constantly debated. Dr. Hatchette mentioned the administration of x-ray in cancer of the breast, prior to and after surgery. Arguments on this point have appeared in the literature for the past twenty-five years and entirely contradictory opinions have been expressed, principally because theories rather than facts have been used as the basis for a decision. We feel that there is conclusive objective proof that the combined treatment yields superior results in cancer of the breast. This can be demonstrated by comparison of five year survival rates in large groups of cases. Dr. Hatchette included carcinoma of the cervix among the conditions that he mentioned. I believe that in all stages of this disease the treatment of choice is radiation therapy, and we might add that the same holds true in other locations, as in intraoral carcinoma and carcinoma of the skin. Radiation efficiently administered will give up the best results in the frequent tumors of these sites. I wish to congratulate Dr. Hatchette again on his paper.

Dr. Peters (New Orleans): What has been your experience with it, whether due to radiation before the operation or not?

Dr. Hatchette (in closing): I do not think that radiation is of help at all. It has been disappointing in my hands to attempt to do much for cancer of the gastro-intestinal tract. I have had no luck

in treatment of cancer of the lung in preoperative radiation. I feel that the patient's chance of survival depends entirely upon a very early diagnosis in these two locations, and getting that patient to the surgeon as fast as is possible for a complete removal of those involved areas; but in cancer in almost any other location, I would say, "Yes," that preoperative radiation is definitely helpful. If nothing else, it will tend, I believe, to prevent spread of the disease and usually it will make the lesion somewhat smaller, so that the surgeon is going to have an easier job. I know many of them feel that if we give preoperative irradiation, we are going to make the operation a much more difficult thing for them. I believe we can give a helpful amount of preoperative irradiation without, necessarily, giving a sufficient amount to cause congestion of the blood vessels locally, and thereby cause a much more difficult operation when the surgeon does get to it.

Does that answer your question?

Dr. Peters: Yes.

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## FUNCTIONAL CONDITIONS OF THE NOSE\*

JOSEPH STAMM, M. D.

NEW ORLEANS

One of the admitted weaknesses of the average American is a propensity for discussing his symptoms and illnesses and, with little or no urging, to supply his own diagnosis. It is amazing how many people complain of "sinus trouble", "sinus headaches" and "post nasal drip". What is more astonishing is that many patients with such complaints are found to be free of organic disease when examined. Unfortunately, the layman is not alone guilty of presumptive diagnoses of organic nasal or paranasal sinus disease. During the War, in Europe, all hospital trains or convoys could be counted on to contain many cases of supposed organic nasal or sinus disease which could not be substantiated, yet all of these cases were evacuated to the zone of communication by physicians.

In a recent article, Dr. Arthur Proetz classically describes his reaction to the symptom of postnasal discharge:

"To the most recent of those repulsive

minor medical bugbears with which the American public delights in saddling itself, it has given an equally repulsive name: "postnasal drip". The term leaves nothing to the imagination. The symptom, on the contrary, leaves everything, which constitutes its chief menace. It brings up the rear of quite a procession of fearsome public enemies: Halitosis; Barber's itch; B. O.; "strep" throat; "athlete's" foot; and some others. Where the term arose I am unable to discover. Overnight the laity taught it to the doctors in hushed and often despondent tones. One hears it a dozen times a day, stigmatized usually with one of those clichés reserved for incurable diseases."

Obviously there is not such widespread organic disease of the nose and sinuses as the frequency of symptoms might indicate. The answer apparently lies in the fact that many of these self-diagnosed diseases are, in reality, an exaggeration or disturbance of normal functional processes.

Briefly, there are three primary functions of the nose: (1) it accommodates the olfactory organ; (2) it conditions the inspired air to the requirements of the pulmonary surfaces by warming, moistening and filtering it; and (3) it cleanses itself of the foreign material which it has extracted from the air. This last named function is at least as important as the rest in health, and is much more so in the control and eradication of infectious disease. In other words, it is the function of the mucus to carry off pathogenic organisms and foreign matter. The excessive mucus or "drip" frequently complained of is evidence in itself of protective activity on the part of the body.

Some of the factors which contribute to abnormalities of nasal function are:

- (1) Allergens—inhaled or ingested
- (2) Physical conditions
  - (a) Central heating
  - (b) Thermal changes
  - (c) Changes in atmospheric pressure—flying, etc.
- (3) Excessive and prolonged medication
- (4) Emotional and metabolic disturbances

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- (5) Endocrine disturbances
- (6) Irritants
  - (a) Tobacco smoke
  - (b) Fumes
  - (c) Dusts
- (7) Alcohol

This is not a complete list. It can be seen at a glance that several factors, contributing to disturbances of function may be present in the same individual. For example, a patient with nasal allergy is frequently guilty of excessive medication in the form of nose drops, sprays or inhalers; and, naturally, his physical surroundings are dynamic.

The diagnosis of functional disturbances of the nose and sinuses is not attended with marked difficulty. Organic disease is first ruled out by means of a careful history and physical examination. Cytologic studies of the nasal secretions are of inestimable value, especially in allergic conditions. Such examinations may be made in ordinary office practice with the expenditure of little additional time and energy.

Because of the prevalence of allergic rhinitis and sinusitis, it is deemed wise to discuss the subject briefly, particularly since some advances have been recently made in therapeutics of these conditions. Hansel describes two major categories in relation to otolaryngology.

*Hay Fever:* The history, clinical findings and cytologic picture make the diagnosis fairly easy. Hyposensitization to offending allergens has been a time honored form of therapy. With proper deference to our colleagues, the allergists, the results have not been uniformly successful. The newer anti-histaminic drugs have proven, in many cases to be a valuable adjunct in the control of acute symptoms.

*Perennial Nasal Allergy:* Synonyms for this condition are vasomotor rhinitis, hyperesthetic rhinitis, etc. Many persons with this condition manifest no seasonal hay fever symptoms, although they may occur in the same individual. These patients occasionally respond well to allergenic hyposensitization, especially to dust extract. McElin and Horton have published encourag-

ing results with the use of the anti-histaminics in this condition.

Any discussion on functional disturbances of the nose would be incomplete without some mention of the excessive use of nose drops. The regrettable practice of continuing the doctor's, or druggist's prescription—intended for a passing ailment—prolongs many nasal symptoms. Drops which act as constrictors cause overventilation and drying. Most constrictors, despite much literature to the contrary, have a secondary reaction of vasodilation which causes congestion and altered secretion. Numerous reports are appearing in the literature of dependency upon the more powerful of the constrictor type of drops. The oily nose drops containing menthol, eucalyptol and similar drugs are sources of constant irritation and inflammation when their use is prolonged.

#### CONCLUSIONS

1. A great number of people who believe themselves afflicted with serious organic disease of the nose or paranasal sinuses, have only mild or disagreeable functional disturbances.

2. Proper recognition of these conditions with an attempt to eradicate the underlying cause is the desirable method of approach.

3. Cytologic examination of the nasal secretions is of value in diagnosis.

4. The newer anti-histaminic drugs appear to offer some help in the treatment of nasal allergies.

5. The prolonged or excessive use of nose drops or sprays is to be discouraged.

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#### DISCUSSION

Dr. W. A. Wagner (New Orleans): I do not want to discuss this paper from the standpoint of physiology, primarily because I am not a physiologist and secondly I could not because it has been such a splendid and thoroughly well presented subject that it leaves little for any physiologist to

discuss. I would like to say a few words from the standpoint of the clinician. As a rhinologist I think it is awfully hard to discuss nasal function without discussing the nasal adnexa. The nose, there is no question of a doubt, is the receptive for the drainage of the sinuses. I remember Servell came out some years ago and described the exacerbation of a chronic sinusitis as a false cold and there was quite a lot of discussion because of misunderstanding but I think he was right when he said "false cold", and that occurred because the nose was the reservoir of drainage of its adnexa, the sinuses. There is no question of a doubt in my mind that the physiology of the nose is altered by the pathologic condition of the sinus. That is confusing to the general practitioner and that is the reason I rise to mention this. When the nose becomes acutely inflamed as in acute rhinitis and acute sinusitis recuperation occurs because of its physiology. The nose having large drainage space between the turbinates and anteriorly and posteriorly, is able to recuperate but the sinus fails in many instances because of such altered physiology to which is added a deviated septum or enlarged turbinate which obstructs the small ostium. This altered physiologic function exists within the nose and is aggravated during infection by pathologic condition in the sinus. It is true that often one can not demonstrate to his own satisfaction physically that such a sinus infection exists and it is there where further study is imperative and unless such a sinus is properly studied by cytologic studies no one can determine the existence of such a sinusitis.

From the standpoint of diet there is no question of a doubt that diet has much to do with the appearance and physiology of the nose. Jarvis, for example, brought to our attention, the fact that a very highly acid diet had altered the physiology of the nose due to altered pathology of the mucosa. That acid diet produced a dry, red looking nose and there was no question of a doubt about that.

Now the question of postnasal drip which we heard the author mention and quoted an authority on it. Every postnasal drip is not a dietary nose. Every postnasal drip is not a sinusitis. Every postnasal drip is not an altered physiologic nose. That nose may be pathologic and the drip may be a result thereof, but whenever a patient complains of a postnasal drip do not stop looking for the cause until you find it. I must admit I can not always find the cause but there is a cause and we should make every effort to find it. When the general practitioner gets a patient whose complaint is postnasal drip he should send that patient to a rhinologist for further investigation, particularly if unable to find some generalized altered physiologic or pathologic state. I think we can be of much service to those who send patients to us.

Dr. Stamm (in closing): I wish to thank Dr.

Wagner for his discussion. We are occasionally accused, in jest, of "specializing" in either the right or left nostril. It is obviously just as impossible to disassociate the nose and sinuses. Their anatomic and functional relationships are intimate.

I have nothing else to add.

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## CLINICO-PATHOLOGIC CONFERENCE\*

CHARLES E. DUNLAP, M. D.†

AND

EDGAR HULL, M. D.††

NEW ORLEANS

The following is a clinico-pathologic conference which was presented before the annual State Medical Society meeting.

### PROTOCOL

M. D., a colored female, aged 24, divorced, was admitted to Charity Hospital in New Orleans on August 20, 1946 and died on September 20, 1946.

*History:* The patient entered the hospital because of throbbing pain in the rectum of five days' duration and chills and fever for four days. She had had no rectal bleeding, abdominal pain, or previous gastrointestinal symptoms. There was no history of cough, dyspnea, sweats, palpitation or chest pain, nor of pyuria, dysuria, burning on urination, or menstrual irregularity. The patient denied venereal disease or previous illness. She had experienced occasional headaches. No family history of tuberculosis, cancer or diabetes was reported. The patient was employed as a maid in a hospital.

*Physical Examination:* Temperature 103.4°; pulse 90; respiration 20; blood pressure 140/70. The patient was a well developed, well nourished colored female appearing acutely ill. Eyes, ears, nose and throat were negative; head was negative. The thorax was well developed. No nodules were felt in the breast and there was no discharge from the nipples. The lungs were clear to percussion and auscultation, the rhythm and sounds of the heart normal. The abdomen was relaxed and non-tender. No masses or enlarged viscera were felt. Extreme tenderness was elicited on palpation of the perineum, just anterior to the rectum; digital examination of the rectum was very painful. On vaginal examination an exquisitely tender mass was felt in the recto-vaginal septum. This mass was opened through the rectum while the patient was in the accident room and proved

\*Presented before the Sixty-seventh Annual Meeting of the Louisiana State Medical Society, May 14, 1947.

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to be an abscess containing some 10 c.c. of thin yellow pus. She was then sent to the ward.

**Laboratory Findings:** Blood: red blood cells 3.68 million and hemoglobin 9.5 gm. per cent on September 10, 1946. Red blood cells 3.9 million and hemoglobin 11.0 gm. per cent on September 12, 1946. White blood cells taken each day from September 10 to September 19 were as follows: 13,900; 6,900; 7,100; 9,9800; 6,000; 13,600; 30,300, and 48,500 on the day before death. Apparently no blood counts were made before September 10, 11 days after admission. Differential counts done by a student showed young cells believed to be of the granulocytic series making up from 14 to 95 per cent of the total white count; proportion of young cells rose terminally. The hematocrit was recorded on three occasions as 22.0, 33 and 30. Kline negative. Urine: Yellow, acid, specific gravity 1.012, albumin negative, sugar negative. Sediment, occasional epithelial cells and crystals. Only two urinalyses are recorded (August 30 and September 3, 1946). No determinations of blood urea or N.P.N. were made. Blood culture on September 13 showed *Staphylococcus albus saprophyticus*—20 colonies per c.c.

**Hospital Course:** The patient was given sulfadiazine gm. IV stat. and gm. 1 every four hours for 24 hours. This had no apparent effect. Penicillin was begun on September 3, 1946, 30,000 units every three hours and continued through September 15, 1946. Sulfathiazole was given from September 4 to September 10. The patient's temperature ranged in irregular fashion between 101.0° and 104.0° throughout her hospital stay. Fluid intake including numerous infusions of glucose and saline ranged from 1000 to 3800 c.c. daily, and output from 2800 c.c. to 300 c.c. Output during the last three days of life was 1000 c.c., 540 c.c. and 600 c.c. on a daily intake of approximately 3000 c.c. During the first few hospital days she vomited a great amount but had no other complaints; there was, however, no improvement in her general condition.

On September 4, crepitation was felt in the rectovaginal septum and gas bacillus infection was suspected. A transfusion of 500 c.c. of whole blood and 40,000 units of polyvalent gas bacillus antitoxin were given. The region of the abscess was again opened through the perineum, evacuating 5 c.c. of foul smelling green pus. A biopsy of the abscess wall showed acute and chronic inflammation and smears showed a "mixed infection including spore forms." Culture was reported as showing staph. aureus saprophyticus, aerobacter, fecal type strep. and aerobic Gram positive and negative rods believed to be saprophytic.

On the next day, September 5, while an infusion was being given, she had an episode characterized by dyspnea and a rapid thready pulse. On September 6 she was very short of breath, there were

rales at both lung bases, and gallop rhythm was noted. On September 7, a tic-toc rhythm was present with a heart rate of 140; venous pressure on this day was 115 mm. of water. An electrocardiogram recorded on September 7 showed sinus tachycardia, small QRS complexes and low T waves in the standard leads, and isoelectric T waves in leads CF 4, 5, and 6. She was digitalized with digitoxin, and on the next day was less short of breath, the heart rate slower. Shortly after midnight on September 9 she began to complain of severe pain in the left axillary region, accentuated by breathing. A friction rub was heard in this region, and rales and dullness were detected over the left lower lobe. The pain was relieved by morphine and did not recur. An x-ray of the chest the following morning showed "shadows at both bases suggestive of scattered infiltrations." The right femoral vein was found to be indurated.

On September 11, the inferior vena cava and both ovarian veins were ligated, and the right lumbar sympathetic chain sectioned. At operation a "firm, cord-like knotty vein was felt in the region of the left uterine artery". During the week following the operation she vomited a great deal; Wangensteen suction was employed. Several transfusions were given during this period. On September 13, after receiving 500 c.c. of blood followed by 1000 c.c. of glucose in saline, marked dyspnea again appeared, which was relieved in 10 minutes after the administration of morphine and oxygen and the application of tourniquets to the extremities. A portable chest x-ray on September 17 showed "suggestive infiltration in the right upper lobe, compatible with pneumonia."

On September 19, the patient had a sudden hemorrhage of about 1000 c.c. from the perineal wound and went into shock; blood pressure was not determinable. The wound was packed and her blood pressure was restored in three hours to 108/50 by the transfusion of 1500 c.c. of whole blood. Within a few hours she lapsed into coma; temperature rose sharply to 104.0°, gasping respiration developed, and she died twelve hours after the onset of the hemorrhage.

#### DISCUSSION

**First slide:** This is the temperature curve during the first week of hospitalization. Although there are fairly wide swings, the temperature is continuous, never going below 101.0°. The swings are probably due to aspirin which she received at frequent intervals.

**Second slide:** This x-ray was taken on September 9, the day on which she complained of severe pain in the chest. There is no definite evidence of consolidation. Rather profuse opacity is noted.

*Third slide:* This is an electrocardiogram made on September 7 or 8, after the patient had complained of shortness of breath and had gallop rhythm. The T-waves are low. Leads CF4, CF5, and CF6 have practically isoelectric T-waves.

*Fourth slide:* This is the final chest plate and was made on September 17, three days before death. It shows a very definite opacity of upper right lung field.

*Discussion by Dr. Hull:* I would like first to enumerate a few unfortunate omissions in the clinical study of this patient which might lead to greater accuracy in the clinical diagnosis and which might have served as guides to more effective therapy.

The most important was the failure to examine the pus from the initial drainage of the abscess. By this omission the best chance of determining the etiologic agent was missed.

Second, no blood count was made early in the patient's illness before complications developed. Therefore, the chance of the white blood count aiding in diagnosis was greatly reduced.

Third, the unusual findings of the student's counts were not checked by an experienced hematologist; hence it is not known whether reliance can be placed upon them.

Fourth, in spite of very low urinary output, and in spite of vomiting which appeared early in the patient's hospital stay, only two urinalyses were made, both during the first few days after admission. Microscopic examination was done on only one of these. Also, in view of these findings, blood urea and blood creatinine determinations should have been made.

Fifth, the final important omission was that only one blood culture was made. Therefore, the chance of discovering the etiologic agent was decreased.

Regarding the etiology, about as far as we can go is to say that this patient's illness was of an infectious nature and it was due to an organism which is not inhibited by penicillin or sulfonamides. The patient received fairly large doses of each of these without any apparent effect. We can say,

therefore, that this infection was not due to hemolytic streptococic or staphylococic or common pyogenic bacteria.

Regarding the anatomic diagnosis, we can say quite definitely that this patient had a perirectal abscess, and because there was no evidence of disease found in the pelvis we can say that the organism entered through the rectal mucosa or blood stream and not from the generative organs. Since the patient's fever continued uninhibited after the drainage of the abscess, it was either a septicemia from the beginning or there was a second abscess which was not drained. The second thing is that the patient had thrombosis of the right femoral and common iliac and left internal iliac veins. From the data at hand we cannot say whether thrombosis occurred primarily in the pelvic veins, due to septic thrombophlebitis, or primarily in the veins of the legs and was due to stasis rather than infection. We can be quite sure that this patient developed pulmonary complications, either embolism or pneumonia, or both. About the status of this patient's heart, I do not believe we can be certain. We can be sure that the function of her heart was embarrassed, at least on the occasion that she developed dyspnea after the infusion and transfusion, but it is impossible to say whether this cardiac embarrassment was due alone to too much salt given as saline and other sodium salts such as bicarbonate given with the sulfonamides, or whether the infection was actually complicated by acute myocarditis. The electrocardiogram is not especially helpful in saying whether or not this patient had an acute myocarditis.

From the functional standpoint, we can say that this patient suffered the deleterious effects of a severe infection, that she suffered impairment of respiratory and cardiac function, and retention of urinary constituents due to inadequate urinary output. Certainly the immediate cause of death was circulatory collapse due to blood loss.

Going into the field of speculation, we may consider the etiology in more detail. What organisms are there which are not inhibited by penicillin or sulfonamides and



which commonly cause perirectal abscess? One is the *Salmonella* group, which sometimes cause septicemia as well. In some *Salmonella* infections there is septicemia without localized symptoms and in some cases there is abscess formation without septicemia. I can say then that organisms of the *Salmonella* group could produce a clinical picture compatible with the one this patient presented. Some of the colon bacilli also produce perirectal abscess, but less commonly septicemia except as a terminal agent. Another organism is the strep. fecalis. It is quite resistant to sulfonamides and penicillin. Finally, I think we should mention the tubercle bacillus. Perirectal abscess is occasionally the first manifestation of tuberculosis and it occurs not uncommonly in individuals in whom pulmonary tuberculosis has previously been diagnosed. It is not definitely known whether it is due to swallowed organisms entering through the rectal mucosa or whether the organisms reach perirectal lymph nodes by way of the blood stream, in which case it would be analogous to tuberculosis of the lymph nodes elsewhere. Could this be tuberculosis of a disseminated type with a localizing perirectal lesion? It should be mentioned as a fairly definite possibility.

Another point: was the thrombophlebitis due to bacterial invasion of veins or merely a phlebothrombosis? We cannot say, but finding the indurated femoral veins would suggest the latter. The third speculation is whether there is a relationship between the ligation of the vena cava and the massive terminal hemorrhage. Certainly ligation causes increase of pressure in the veins which drain into the vena cava. It might be considered possible that increased pressure in the veins of the perineum might have been a contributing factor in the massive hemorrhage from the perineal wound.

Next, the peculiar blood picture: Was it due to a very severe infection, or was it a leukemoid reaction to sulfonamides, or were the counts erroneous? I don't know. Another thing on which we might speculate: was this a gas bacillus infection? I think not. *B. welchii* were never isolated

from the pus, and crepitation was not discovered prior to the initial drainage. Probably gas forming bacilli entered after incision,—members of the colon group, strep. fecalis, and so on.

I think I should be called upon to make a final diagnosis and I will say that this patient had an infection due to an unknown organism, most likely one of the *Salmonella* group or the tubercle bacillus. From an anatomic standpoint, she had an abscess in the recto-vaginal septum, phlebothrombosis, pulmonary infarction and pneumonia. Whether or not she had acute toxic myocarditis, I do not know. As regards the cause of death, I should say that the immediate cause was hemorrhage and that contributing causes were a septic state and impairment of respiratory and cardiac function.

My closing remarks will be brief. Regarding the rapidity with which the tuberculous process in this patient's lungs spread, there was an x-ray made two or three days after admission. I did not have it reproduced because it was overexposed, but one could be reasonably sure that at that time there was no extensive process in this patient's lung. The second one taken prior to patient's death showed definite opacity of the right upper lung field.

The second point that I want to reiterate is that an error of omission that prevented us as clinicians from making an etiologic diagnosis was also responsible for the inability of the pathologist at postmortem examination to determine the organism responsible for the abscess. The greatest omission was neglect to culture the pus obtained from the abscess on admission. The nature of the organism might have dictated the type of therapy.

The final point: in the therapy of mixed infections which enter the tissues from the gastrointestinal tract, it has been shown that combined therapy with penicillin and streptomycin gives results that are superior to those obtained with the use of the streptomycin or penicillin alone. If this patient had been given streptomycin as well as penicillin, the perineal infection might have

been brought under control, and almost certainly the flare-up of the tuberculosis would not have occurred.

*Dr. Dunlap:* When the body of this young colored woman came to autopsy it was not emaciated or dehydrated. One of the difficult tasks in the management of a long febrile illness is the maintenance of adequate hydration and general nutrition and the physicians and nurses who were responsible for this patient deserve credit for excellent general care.

Externally the body showed few signs of serious disease. The abdominal incision that was made for the ligation of the ascending vena cava was well healed and showed no evidence of infection. There was a ragged defect in the perineal skin at the site of drainage of the pelvic abscess. The defect opened into a region of necrotic friable tissue which extended into the perineal fat and communicated through a small fistula with the rectum. Further investigation of this region showed extensive necrosis of the perineal soft tissues and several small abscesses which had not been drained. On opening the peritoneal cavity no free fluid was encountered and there was no evidence of active or healed peritonitis. Healed surgical incisions were present in the peritoneum on both sides of the pelvic brim where the ovarian veins had been ligated and a larger incision in the peritoneum of the right gutter where the cecum and colon had been freed and reflected medially in the ligation of the vena cava. The abdominal viscera were not remarkable.

The left pleural cavity contained 300 c.c. and the right 200 c.c. of clear yellow fluid. Pleural effusion totaling 500 c.c. should not cause serious respiratory embarrassment but it is worth mentioning that we frequently find pleural effusions at autopsy, large enough to serve as a contributory cause of death and all too often there is no clinical record that the effusion was detected during life. This patient had no pleural adhesions and no exudate was present on the pleural surfaces. The right lung weighed 500 grams which is considerably more than normal and the left lung 320 grams which

is only a little above normal. There was boggy hyperemia and edema of the bases of both lungs and a nodular consolidation 3 cm. in diameter in the right upper lobe which on external examination was thought to represent an infarct. However when the region of consolidation was opened its central portion showed extensive caseation necrosis typical of tuberculosis with a broad surrounding zone of tuberculous pneumonia. I am surprised that Dr. Hull suspected the presence of tuberculosis on the basis of such meager clinical evidence but he was certainly correct.

The heart weighed 260 grams which is within normal limits for a woman of this weight (130 pounds). No abnormalities were found grossly or microscopically in the myocardium, valves or coronary vessels. In view of the clinical findings we made a particular search for myocarditis but none was found.

The liver was dark purple, bloody and considerably enlarged, weighing 2060 grams. The gall bladder was not remarkable. Throughout the gastrointestinal tract from the stomach to the rectum there were scattered petechiae of the mucosa but the only important changes were in the rectum and perirectal tissues. The rectum was filled with dark red, clotted blood and the posterior rectal wall was friable and necrotic and showed yellow-green and black discoloration. Three centimeters above the anal sphincter a fistula extended posteriorly through the rectal wall into the region of perineal infection and necrosis. There was no gross evidence of tuberculosis in this region.

The right kidney weighed only 80 grams while the left kidney was moderately enlarged and weighed 340 grams. The right kidney was a mere shell of fibrous tissue surrounding a distended, pus-filled pelvic cavity. The kidney parenchyma had been almost completely destroyed. These changes are practically diagnostic of an old, chronic, progressive pyelonephritis. A double ureter was present on the right kidney and this congenital anomaly helps to account for the unilateral pyelonephritis. The left kidney



showed slight edema of the cortex and minimal pyelitis. Its increased size and weight are best explained as a compensatory hypertrophy which developed over the course of years as the function of the opposite kidney was gradually destroyed.

The spleen weighed 530 grams which is several times the normal weight. It was soft and hemorrhagic and contained several yellow infarcts which I am not able to explain satisfactorily. The aorta was normal. The ascending vena cava was ligated just above its bifurcation but a residual lumen 2 mm. in diameter persisted at the site of ligation. Below this level the lumen was of normal caliber and was filled with a homogeneous dark red blood clot such as one would expect to form as a result of ligation of the vessel. Pale, grey laminated clots were present at the level of the iliac bifurcation and extended for a short distance into the iliac vessels. These thrombi must have been present before the ligation since they are of the type that can form only in a moving stream of blood. No thrombosis was present in the vena cava above the level of ligation. It was particularly interesting to find that the large veins of the thigh were free of thrombi indicating that blood in these veins had succeeded in finding anastomotic channels sufficient to maintain good return flow even after the vena cava had been occluded. Both ovarian veins were ligated and thrombosed and occasional thrombi were present in the retroperitoneal pelvic veins. The intensive chemotherapy may account for the fact that no suppurative thrombi were found.

Microscopic examination of tissue from the rectovaginal abscess showed extensive suppuration and tissue necrosis. Smears and culture of this tissue showed a variety of bacteria as might be expected from the fact that there was free communication with the lumen of the rectum and the perineal skin. Careful study revealed no evidence of tuberculosis in the rectovaginal tissues but in sections of the lung there was an actively spreading caseo-nodular tuber-

culosis. Segments of an old fibrous capsule from a previous lesion could still be identified but the active spread beyond this capsule was not exciting an effective fibrous reaction. It seems fairly certain that the tuberculous lesion in the right upper lobe represented a reactivation of an old arrested lesion. An additional microscopic finding of some interest was extensive extramedullary hematopoiesis in the liver. Blood cell formation in the liver is normal during fetal life but hematopoietic tissue disappears from the liver shortly after birth. During periods of rapid or continued blood cell destruction such as must have occurred in this patient the liver may resume its function of blood formation. The only other microscopic finding which deserves mention was the presence of tiny, scattered focal necroses in the brain. Lesions of this character may result either from direct toxic injury or from anoxemia. In this patient either toxemia from the pelvic or anoxemia from the terminal hemorrhage could have been responsible.

In summary, I agree with Dr. Hull that the immediate cause of death was hemorrhage and shock in a patient who was already extremely ill from an uncontrolled rectovaginal abscess. Treatment was heroic but ineffectual. There were two attempts at surgical drainage of the abscess but at the time of autopsy there were several unopened pockets of pus. A large total dose of 6,560,000 units of penicillin was given and this may account for the fact that no sepsis was found except in the region of the abscess. Failure of chemotherapy to control the local lesion is not surprising in view of the mixed bacterial flora and the large bulk of necrotic tissue. Penicillin in the circulating blood is not carried into ischemic tissues in effective concentrations and in treating infections in devitalized tissue it may be wise to raise the blood level of penicillin well above the ordinary effective range in the hope that effective concentrations of the drug will seep into the infected region. Even in mixed infections

penicillin can serve a useful purpose in destroying sensitive organisms thus improving the chances that the body can handle those that are penicillin resistant.

Ligation of the vena cava and ovarian veins was probably justified in view of the clinical findings but it must have taken considerable surgical courage to operate on a patient in such poor condition. The focus of active tuberculosis in the upper lobe of the right lung had not reached large size but does serve as a reminder that reactivation of arrested tuberculous lesions may occur in any prolonged, severe illness.

I believe that this patient still had a fair chance of survival up until the time of the severe hemorrhage shortly before her death. The pelvic infection, although not controlled, had been limited. The sustained fever suggests that microorganisms were gaining access to the blood stream but they were not able to establish suppurative foci in distant parts of the body. The heroic efforts which were made to save this woman's life might well have succeeded had it not been for the unfortunate and unpredictable fatal hemorrhage.





The Journal Committee wishes to announce the appointment of an Editor for the Journal in the person of Dr. Philip Harold Jones. It is felt that with Dr. Jones' known ability, energy and loyalty to the principles of the practice of medicine and organized medicine we can be confident that the new appointee will meet the requirements and responsibilities of this important office.

Dr. Philip Harold Jones was born on February 26, 1896, in Jackson, Louisiana, the son of Annabelle Smith Jones and the late Dr. Philip Huff Jones of Baton Rouge. His family moved to Baton Rouge in 1907, where his father practiced medicine and lived a life of public usefulness until his retirement, about ten years before his death in 1946 at the age of ninety-one.

Dr. Philip Harold Jones attended the Baton Rouge High School and received his B. A. degree from the Louisiana State University in 1916. He was graduated from the Tulane University of Medicine in 1920, and was the third generation of his family, in direct descent, to receive an M. D. from Tulane; his grandfather, Dr. John Welsch Jones, in 1852, and his father, in 1878, having preceded him.

He served as an intern at Charity Hospital for June, 1920, until September 1, 1920, and left to accept an appointment as a Rhodes Scholar. He studied at Oxford University, England, for four years, and earned the degree of Ph. D. in pathology in 1924. While abroad, he also studied in the clinics of Vienna, dermatology in the Hospital St. Louis, Paris, and cardiology in the London Hospital and the London Heart Hospital. He returned to the Charity Hospital in New Orleans and finished his internship in 1925. He was House Physician at Charity Hospital from 1926 until July, 1928. In the summer of 1928, he studied psychiatry for two months at the East Louisiana State Hospital.

During the year 1928-1929, Dr. Jones was a full-time instructor in medicine at Tulane, and from 1928 to 1937, a part-time instructor. In 1937, he was appointed assistant professor of clinical medicine, and is now an associate professor. In 1929, he commenced private practice, specializing in internal medicine.

He has held various offices in the Orleans Parish Medical Society, and was president in 1945. He has also served in many capacities in the Louisiana

State Medical Society and is now a member of the Executive Committee. He is a member of the American Medical Association, the Southern Medical Association, and the Lafourche Valley Medical Society. He is a fellow of the American College of Physicians, and was certified by the American Board of Internal Medicine, July 1, 1938. He is a member of the Nu Sigma Nu and the A.O.A.

During the first World War, he was in the

S.A.T.C. at Tulane University, and in World War II, he was an examining physician for the local Boards and a member of Medical Advisory Board No. 1, and assistant Chief of Medical Service in the emergency unit formed at Charity Hospital.

He is the author of numerous medical articles published in leading journals and of a series of chapters on infectious diseases published in a reference book on medicine.



## NEW ORLEANS

## Medical and Surgical Journal

*Established 1844*

Published by the Louisiana State Medical Society under the jurisdiction of the following named Journal Committee:

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## THE SITUATION IN REGARD TO NURSING CARE

The supply of professional nursing care does not meet the needs of the sick.

The situation has received attention of the American Nurses' Association and of many other organizations. The principal causes are found in the dislocations and alteration in the pattern of human effort caused by the war. Additional causes are the transition from 12 hours to an eight hour day; the increase from 1,226,000 hos-

pital beds in 1940 to 1,738,000 in 1945, the increase in population, and the enhanced desire for nursing service under conditions of full employment.

The present number of registered nurses is 318,000 and is the largest in the nation's history. It is reported that one third of these have entered into other fields. Probably another third are employed in teaching, industrial and executive positions. The remaining third need to be supplemented by 42,000 to meet the needs of today. Where are these to come from? In 1945, for example, 1,295 schools of nursing reported a freshman enrollment of 56,567. In 1946 the freshman enrollment in 1,271 schools was only 30,899. Figures for 1947 indicate an even greater drop for that year. After a careful survey by an authoritative group it was stated that "The general belief seemed to prevail that the nursing profession is desirable but that it offers too little reward to those who practice it and too high a cost to those who need it. This is like the situation in which an irresistible force meets an immovable object. How to reconcile the two aspects of this situation is an exceedingly difficult problem."

The American Nurses' Association has a program to hold nurses in the profession and to attract prospective recruits.

"On the state level today the ANA seeks amendments to the present nurse practice acts to bring about:

"1. Uniformly high standards of preparation for professional nurses.

"2. Provisions enabling nurses licensed in one state to secure more easily registration in another, an important point in remedying the present faulty distribution of nursing services.

"3. A thorough overhauling of the system of professional nursing education to eliminate exploitation of student nurses and to give them a broader academic education as a basis for the professional nursing program.

"4. The regulation of approved schools of practical nursing, and a stricter definition of the function of the practical nurse.

"5. Compulsory licensing of both professional and practical nurses.

"On the federal level the ANA is today urging the enactment of legislative measures to:

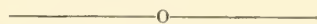
"1. Extend to nurses the benefits of coverage under the Social Security Act, the Federal Unemployment Tax Act and the Federal Insurance Contribution Act.

"2. Extend Federal Old Age and Survivors Insurance to those nurses who are self-employed.

"3. Equalize the retirement benefits of nurse veterans of World War I and World War II.

"4. Insure to professional employees full freedom of choice in the selection of bargaining representatives."

The influence of such a program upon the total number of available nurses will be slow. To supply a part of the need the use of practical nurses is much discussed. The requirements and methods to this end are not agreed upon. In a condition where the pressure for their utilization will increase it would be well for the interested parties to formulate a program.



#### THE NEW ORLEANS GRADUATE MEDICAL ASSEMBLY

The New Orleans Graduate Medical Assembly will have its eleventh annual meeting February 23-26, 1948. This organization which sponsors the meeting is composed of New Orleans physicians who desired to bring to the doctors of this section another annual meeting in medicine which would be informative and helpful. They are to be congratulated on the success attained. The first session was attended by 511 physicians. For the 1947 session 1022 physicians registered and over 400 were regretfully rejected because of lack of hotel space.

The coming meeting gives every promise

of being attractive and successful. Papers in fourteen fields of specialization are to be presented by sixteen eminent visiting speakers. The subject matter is being arranged so as to be of value to the practitioners. It is felt that those in attendance this year, as in the past, will find that each paper gives them something to take away in the field of helpful knowledge.

This year, as last, a post-clinical tour is being arranged. Those who wish to take a vacation in the winter under conditions of agreeable company and interest can enjoy the 15 day trip by plane to the historic points in Central America. On Saturday, February 28, a party composed of doctors and their wives, will leave by Pan American Clipper for Merida, Yucatan. After a four-day visit they will fly to Guatemala City, Guatemala. While in Merida many places of medical and historical interest will be visited, including some of the best preserved ruins of the Mayan empire and civilization.

Following these delightful days of companionship and sightseeing, a medical program will be presented in Guatemala City. The sightseeing schedule will then continue in various directions from Guatemala City, the last day and a half of the trip being unscheduled to permit additional side trips or entertainment in the city as may be desired.

Departure from New Orleans will be on Saturday, February 28, and the group will return on Friday, March 12.

Details and a complete itinerary are available at the office of the Assembly, Room 105, 1430 Tulane Avenue, New Orleans.

Dr. Joseph D'Antoni, President; Dr. Max Green, Secretary; Dr. Edgar Hull, Director of Program, and other officers are to be congratulated on having planned so inviting a program.



## ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

***An informed profession should be a wise one.***

### MEDICAL DEFENSE

From information received at the office of the State Society, it has been learned that there is some misunderstanding on the part of many members of the organization in regard to the benefits offered by the State Society through medical defense in connection with malpractice suits brought against members. In order that there may be clarification of the privileges offered in regard to medical defense there should be borne in mind two separate and distinct objects.

First, the Louisiana State Medical Society, through medical defense, undertakes to defend its members against suits, threatened or otherwise, after approval of defense by the Committee on Medical Defense. This comprises the services of a lawyer, court costs and expert witnesses if the case is brought to trial. The services of the attorney are furnished also for any deliberations or services in regard to settlement or adjustment in connection with threatened claims previous to suit. Every active member is entitled to this service with no extra cost.

Second, if a case goes to trial or if in an agreement certain indemnity is agreed upon or assessed against the doctor by the court after due trial, the State Society is not obligated to pay such indemnity. For this there has been arranged a group liability policy which furnishes the individual doctor, at a nominal cost, such indemnity in cooperation and under the supervision of the Medical Defense Committee of the State Society. To undertake to pay indemnity for judgment by the State Society would involve three problems: (a) It would be inequitable for the membership at large for the Society to assume payment of judgment amounting anywhere from \$500.00 to \$50,000.00 against an individual doctor because the percentage of such cases is comparatively small in relation to the total

membership. (b) Obviously the finances of the Society would have to be greatly increased to take care of such a financial burden. The uncertainties of this cost would create a very unsteady situation in economic status of the organization. (c) To issue such protection in the form of indemnity to meet such judgments would make it necessary for the State Society to comply with the State Insurance laws, which would require that the organization be incorporated as an insurance company. In other words it would mean that the organization would go into the insurance business. Further, it would be necessary to meet the requirements of the Social Security and Internal Revenue laws concerning such corporations.

In view of the above the State Society has endeavored to do the next best thing, by arranging with a national insurance company to handle a group malpractice policy at a reduced premium rate and the company has the responsibility of meeting the payment of judgment against any members who carry such insurance.

For information it should be stated that the State Society is very proud of the medical defense feature of the organization and particularly so because of the fact that no case ever defended by our group has ever been lost in the State of Louisiana.

Following is a letter received from the Aetna Casualty and Surety Company concerning our present group policy, which we hope will clarify some of the features of the policy which have not previously been understood by some of our members.

Dr. P. T. Talbot, Secretary  
Louisiana State Medical Society  
1430 Tulane Avenue  
Dear Doctor:

There are several aspects of the handling of the Group Professional Liability policy for the Louisiana State Medical Society which may need some clarification. For-

merly the insurance was written by another company whose method of writing the coverage varied somewhat from that of the new carrier. However, the benefits afforded under the two contracts are basically the same.

As you know, the former carrier withdrew from the risk due to adverse experience and it was, therefore, necessary to secure another outlet with another nationally known stock company, the Aetna Casualty and Surety Company. This company has pioneered this field and is presently writing some eighty per cent of all this class of business in the United States.

In the past the rates were variable as respects the type of practice, i.e.; some doctors paid more than others due to their handling of plastic cases, etc. Under the Aetna contract all rates are uniform. If a physician handles x-ray therapy, there is an additional premium for this protection provided that such coverage is desired. It is not mandatory.

There are doubtless some companies who are now offering insurance of this class at somewhat lower rates, but that has always been the case. This is generally the case as respects Roentgenologists. However, the Aetna has the experience and facilities to properly handle this type of insurance. After all, when dealing with such intrinsic items as the reputation of a physician, it is highly desirable that the insurance company be fully competent to dispose of the matters which arise with great care.

Where two or more doctors are acting as a bonafide partnership or where they employ another doctor, then it is essential that this relationship be protected by a partnership policy. This coverage was formerly provided under one policy, including the insured doctors Malpractice insurance and the rates were commensurately higher. The fact that the Aetna provides this coverage in a separate policy may have caused some confusion; however, the provisions are practically the same. There are many legal cases which set the necessary precedence to show the need for this coverage. One doctor can be held liable for the acts of his

partners simply because of the partnership relationship. Claims have arisen where one was enjoined in a suit because of the acts of his partner and yet he had absolutely no knowledge of what has taken place.

Of course, where a doctor or group of doctors may operate a clinic or hospital, it is necessary to provide for this coverage under our regular Proprietors Professional Liability policy or our Hospital policy.

It is our present intention to have a representative of the Aetna Casualty and Surety Company present at the next meeting of the Louisiana State Medical Society in Monroe, Louisiana. Any questions which you may have will be answered at that time if it is at all possible.

Very truly yours,

James H. Thomas,  
Agency Supervisor

—o—

## MEDICAL CARE FOR VETERANS

Recently an appeal was made through the Journal for physicians and parish and district societies to forward to the State Society office complaints received by them in regard to the present contract for medical service for veterans with service connected disabilities, now in effect between the State Society and the Veterans Administration. There has been some attempt by the Veterans Administration to disregard some of the provisions of the contract and these are summed up as follows:

First, patients have been instructed to go to the Veterans Facilities for refill of prescriptions or for the performance of surgical procedures already instituted by a doctor in keeping with the contract; for example pneumothorax cases have been required to go to Veterans Facilities for handling.

Second, there has been an attempt made by some of the regional officers to secure participation of physicians direct with the Veterans Administration rather than as a group from the State Medical Society, which was the aim and the purpose of the contract. In conference with General Hawley, Medical Director of the Veterans Ad-



ministration, recently in Chicago, he denounced such practice and promised to have it corrected.

Third, there is some complaint that this plan, known as the "Hometown Plan for the Medical Care of Veterans" is simply a misnomer because of the fact that the only hometown medical care authorized by one of the regional offices has been examination to determine whether the patient needs hospitalization in the Veterans Facility. This, of course, is contrary to the spirit of the contract.

Fourth, there has been some slowness in payment of bills for services rendered by accredited physicians in private hospitals. This has been especially true in one tuberculosis hospital where the bills have accrued over a period of nine or ten months.

These observations are presented for information of members of the Society and in order that a proper solution may be reached for such services in the future. It was never intended by this contract for such practices to exist under the "hometown" medical service for veterans.

## TRANSACTIONS OF ORLEANS PARISH MEDICAL SOCIETY

### CALENDAR OF MEETINGS

- Jan. 12, Installation meeting, Orleans Parish Medical Society, Jung Hotel, 7:30 p. m.
- Jan. 13, Special scientific meeting, Orleans Parish Medical Society, 8 p. m.  
Orleans Parish Radiological Society, 7:30 p. m.
- Jan. 14, Woman's Auxiliary, Orleans Club, 3 p. m.  
Touro Infirmary Staff, 8 p. m.
- Jan. 15, Veterans Administration Hospital Staff, 8 p. m.
- Jan. 16, The Orleans Society of X-ray Technicians, 7:30 p. m.  
Executive Committee, Hotel Dieu, 8 p. m.  
Lakeshore Hospital Staff, 8 p. m.
- Jan. 19, Hotel Dieu Staff, 8 p. m.
- Jan. 20, I. C. R. R. Hospital Staff, 12:30 p. m.  
Charity Hospital Medical Staff, 8 p. m.
- Jan. 21, Charity Hospital Surgical Staff, 8 p. m.
- Jan. 22, Clinico-pathologic Conference, Touro Infirmary, 12 noon.
- Jan. 26, Scientific and Executive meeting, Orleans Parish Medical Society, 8 p. m.  
DePaul Sanitarium Staff, 8 p. m.
- Jan. 27, Baptist Hospital Staff, 8 p. m.
- Jan. 28, Catholic Physicians' Guild, 8 p. m.  
French Hospital Staff, 8 p. m.
- Jan. 30, New Orleans Hospital Dispensary for Women and Children Staff, 8 p. m.
- Feb. 2, Board of Directors, Orleans Parish Medical Society, 8 p. m.
- Feb. 3, Eye, Ear, Nose and Throat Staff, 8 p. m.
- Feb. 4, Mercy Hospital Staff, 8 p. m.
- Feb. 5, Clinico-pathologic Conference, Touro Infirmary, 12 noon.  
Executive Committee, Baptist Hospital, 8 p. m.

N. O. Society of Anesthesiologists, Charity Hospital, 8 p. m.

Feb. 6, Foundation Hospital Staff, 8 p. m.

### NEWS ITEMS

Dr. J. Kelly Stone was elected president-elect of the Society to take office as president in 1949, in balloting Saturday, December 13 at the Society's office. Dr. Stone will serve as president-elect for one year, succeeding Dr. Max M. Green, who was elected last year, and who will assume the duties of president in 1948.

Other officers elected were: Dr. C. J. Brown, first vice-president; Dr. J. O. Weilbaecher, Jr., second vice-president; Dr. John Menville, third vice-president; Dr. N. J. Tessitore, secretary; Dr. Boni J. De Laoreal, treasurer; Dr. Eugene H. Countiss, librarian; Drs. E. L. Leckert and Chas. B. Odom, additional members to the board of directors.

Dr. H. Ashton Thomas, the retiring president, will also serve as a member of the board of directors during 1948.

Elected delegates to the Louisiana State Medical Society for 1948-1949 were: Drs. George C. Battalora, C. J. Brown, Donovan C. Browne, W. R. Buffington, Wm. B. Clark, Sidney M. Copeland, Lucien A. Fortier, Aynaud F. Hebert, Sam Hobson, John J. Irwin, Theo. F. Kirn, Edwin H. Lawson, E. L. Leckert, Edward Matthews, Joseph P. Palermo, Wm. H. Roeling, J. Kelly Stone, H. Ashton Thomas and J. O. Weilbaecher, Jr.

Installation ceremonies will be held Monday, January 12, 1948 following the annual banquet at the Jung Hotel.

Dr. George Burch, chairman of the Tulane department of medicine, delivered the annual lecture before the Washington, D. C. Heart Association, November 12 in Washington. Dr. Burch also served

as guest lecturer at the University of Southern California and University of Utah medical school before leaving for Washington.

Dr. W. D. Beacham, associate professor of clinical gynecology and obstetrics, was elected secretary of the National Federation of Obstetric-Gynecologic Societies. The term of office is for two years. Dr. Beacham is president-elect of the New Orleans Obstetrical and Gynecological Society.

Dr. Alton Ochsner, the William E. Henderson Professor of Surgery, Dr. Ernest Carroll Faust and Dr. Joseph S. D'Antoni of the department of parasitology took part in the Second Mexican Congress of Medicine held November 7-17 in Mexico City. Dr. Ochsner presented a paper on "Hepatic Amebiasis"; Dr. Faust spoke on "A Present Day Assessment of Tropical Diseases and Tropical Medicine in the United States and Canada" and "Possible Determinants of the Pathogenicity of Endamoeba Histolytica" and Dr. D'Antoni read a paper on "Therapy of Hepatic Amebiasis."

Dr. J. W. Atkinson recently took a post graduate course in general practice at The New York Polyclinic Graduate Medical School.

While in New York Dr. Atkinson attended the New York Academy of Medicine Program.

Dr. William B. Clark served as an associate on the American Board of Ophthalmology in Chicago, October 9-11.

Dr. Clark presented a moving picture on Onchocerciasis in Guatemala on the scientific program, eye section, of the American Academy of Otolaryngology and Ophthalmology in Chicago, October 12-17.

Dr. F. L. Jaubert and Dr. Waldo Treuting participated in the program of the Louisiana Society for crippled children at their annual state convention, in New Orleans, November 22-23.

Dr. Robert A. Katz has returned from England and the Continent, where he has been for the past two months. While there, he reported on his researches on Arteriosclerosis.

On November 2 and 3, Dr. Katz presented, in Chicago, to the American Society for the Study of Arteriosclerosis, two addresses: "The Status of Arteriosclerosis in Europe"; "Intravenous

Ether, A New Approach to the Therapy of Arteriosclerosis".

Dr. T. A. Watters read a paper on "Emotional Implications of the Eye" at the North Carolina Neuropsychiatric Association, Durham, October 31.

Dr. B. Bernard Weinstein presented a paper for the Alabama History of Medicine Society in Birmingham on November 7, entitled "Three Men from Padua".

Drs. Eugene H. Countiss, Isadore Dyer, C. Gordon Johnson, E. L. King, John Weed, and B. Bernard Weinstein attended the Central Association of Obstetricians and Gynecologists held in Louisville in October.

Drs. Weinstein and Weed presented a paper on "Amoebic Vaginitis" at the meeting.

At the November meeting of the New Orleans Gynecological and Obstetrical Society, at the Metairie Country Club, the following program was presented:

"Introductory Remarks" by Dr. Earl Conway Smith, president.

"Hyperemesis Gravidarum" by Dr. Curtis Lund.  
"Heartburn in Pregnancy" by James H. Ferguson.

The next meeting of the Society will be held Thursday, December 11, 6:30 p. m., Metairie Country Club.

At a meeting of the National Conference of Catholic Charities in New Orleans, October 13, Dr. Edmund Connely presented a paper on "Mental Hygiene and its Place in the Community."

Dr. Russell L. Holman, professor of pathology, attended the second meeting of the American Society for the Study of Arteriosclerosis in Chicago, November 2-3, and participated in a panel discussion on diseases of blood vessels. Dr. Holman is engaged in research on the relation of diet to arteriosclerosis, financed by a grant from the John and Mary Markle Foundation.

Dr. Neal Owens, professor of clinical surgery in charge of plastic surgery at Tulane, was elected president of the American Society of Plastic and Reconstructive Surgery at a recent meeting of the group in San Francisco.



## LOUISIANA STATE MEDICAL SOCIETY NEWS

## C A L E N D A R

## PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

EAST AND WEST FELICIANA BI-PARISH  
SOCIETY

The East and West Feliciana Bi-Parish Medical Society met in Clinton at the Baptist Church, December 3, 1947, at which time an excellent dinner, prepared and sponsored by the Clinton Infirmary and supervised by Mrs. Willie B. Hubbs, Mrs. Bentley and Miss Sue Palmer, was served. The following officers were elected by the society to serve for 1948: Dr. C. J. Wise, Angola, President; Dr. W. J. Roberts, Woodland, Vice-President; Dr. E. M. Toler, Clinton, Secretary-Treasurer. Dr. E. M. Toler was elected delegate to the State Society meeting and Dr. Glenn J. Smith was elected alternate.

Dr. Courtland Smith, of Baton Rouge, presented a paper on conjunctivitis which was very favorably discussed by the physicians present and a vote of thanks was extended him for this contribution.

At this meeting Dr. J. F. Dinan, of the East Louisiana State Hospital, was elected a member of the society and a vote of thanks was extended to the Clinton Infirmary and the Staff for the excellent entertainment and dinner.

The next meeting will be held at the East Louisiana State Hospital on the first Wednesday in March, 1948.

## WEBSTER PARISH MEDICAL SOCIETY

At a meeting of the Webster Parish Medical Society on December 9 at the Minden Sanitarium, Minden, the following officers were elected for 1948. Dr. T. A. Richardson, President, Dr. E. S. Rogers, Vice-President, Dr. S. M. Richardson, Jr., Secretary-Treasurer, Dr. C. M. Baker, Delegate to State Society, Dr. W. C. Gray, Alternate. After the election Dr. W. C. Gray presented two colored movies. The first was a partial resection of the stomach and the second was a Wertheim operation. Dues for the coming year were received.

## FIFTH DISTRICT ELECTS DR. COON

A meeting of the Fifth District Medical Society was held on Thursday, December 11, 1947, in the

Virginia Hotel at Monroe, Louisiana. Members of the Fifth District elected Dr. H. S. Coon of Monroe as their president and Dr. Fred Marx of Monroe was named secretary-treasurer. Dr. Coon succeeds Dr. Ralph King of Winnsboro, the immediate past-president of the District. Dr. King was elected as a delegate to the House of Delegates of the Louisiana State Medical Society, scheduled to meet in Monroe in its annual meeting in April, 1948. Dr. C. P. Gray, Jr. of Monroe, President of the Ouachita Parish Medical Society, was named as an alternate delegate.

Presenting papers at the meeting were Dr. Edgar Hull of New Orleans, professor of medicine at L. S. U.—“Recent Advances in the Treatment of Heart Diseases”; Dr. Barrett Kennedy of New Orleans, associate professor of dermatology at L. S. U.—“Skin Rashes Due to Drug Administration”; and Dr. Donovan C. Browne, professor of clinical medicine at Tulane Medical School—“Value of Proctoscopic Examination”.

Other speakers at the meeting included Dr. Gilbert C. Anderson of New Orleans, President of the Louisiana State Medical Society, who spoke on “Malpractice Insurance”, and on “The Growth of Louisiana Physicians Service”, the surgical and obstetrical care plan sponsored by the State Society. The program also included Dr. P. T. Talbot of New Orleans, Secretary-Treasurer of the State Society, and Frank Lais, Jr., Executive Director of the Council on Medical Service and Public Relations and Louisiana Physicians Service. Mr. Lais spoke on “The Proposed Public Relations Program of the Council on Medical Service and Public Relations”.

## SCIENTIFIC EXHIBIT

At the 1948 meeting of the Southern Medical Association, recently held in Baltimore, an exhibit entitled “Effects of Beta-radiation in Ophthalmology: Ciliary Body of Rabbits” was presented by Miss Aleta Barber, Dr. Louis Breifeilh and Dr. George M. Haik. The exhibit concerned work car-

ried out at the Louisiana State University School of Medicine.

#### NU SIGMA NU—RUDOLPH MATAS LECTURESHIP

The Beta Iota chapter (Tulane) of NU SIGMA NU Medical Fraternity is inaugurating an annual lectureship in honor of its most famous member, Dr. Rudolph Matas, Professor of Surgery Emeritus at Tulane and probably the most widely acclaimed living physician. This lectureship is to be known as the "NU SIGMA NU—RUDOLPH MATAS LECTURESHIP", and each year it is planned to bring some outstanding physician to New Orleans to deliver an address. The first lecture will be held on January 28, 1948 at 8:00 p. m. in the Hutchinson Memorial Auditorium of the Tulane Medical School. The organization is fortunate in being able to have Dr. Alfred Blalock, an eminent vascular surgeon and Professor of Surgery at Johns Hopkins Medical School, as the inaugural speaker. His subject will be "Surgical Treatment of Congenital Cardiovascular Defects" with accompanying slides and movie film.

All members of the medical profession are cordially invited to this lecture.

#### AMERICAN COLLEGE OF SURGEONS

Dr. Arthur W. Allen, President of the American College of Surgeons, announces six Sectional Meetings scheduled for 1948, for Fellows of the College, the medical profession at large, and hospital personnel. Each meeting will be two days in length and will include conferences for hospital personnel as well as sessions for the medical profession. The showing of medical motion pictures will begin each day's program at 8:30 a. m. There will be luncheon meetings each day and a dinner meeting on the first evening. The latter will be followed by a symposium on cancer. Panel discussions on scientific subjects, led by internationally known authorities in each field of surgery, will be held each morning and afternoon. The list of meetings follows:

Toledo, January 20 and 21, Commodore Perry Hotel.

Atlanta, January 26 and 27, Ansley Hotel.

Oklahoma City, January 30 and 31, Oklahoma Biltmore Hotel.

Denver, March 1 and 2, Cosmopolitan Hotel.

Minneapolis, March 15 and 16, Hotel Nicollet.

Halifax, May 17 and 18, The Nova Scotian.

Among the subjects to be discussed at the scientific sessions will be fractures of the upper and lower extremities; pediatric surgery; importance of the use of blood and fluids and of adequate nutrition in surgery; early diagnosis and proper treatment of cancer; organization and functioning of cancer clinics and cancer detection centers; intestinal obstruction; management of wounds, surgi-

cal incisions and fresh traumatic wounds; urologic surgery; plastic surgery; vascular surgery; and panel operations on elderly patients with special reference to the reduction of surgical risk.

Among the subjects which will be discussed at the hospital conference will be the increasing use of hospitals; expansion of hospital facilities; higher standards of training for hospital administrators; improvement in personnel policies; increasing cost of hospital service; better rural hospital service; coordination of hospital with other health and welfare activities in the community; Blue Cross and medical service plans; decreasing average days' stay in hospitals; participation of hospitals in cancer control; advances in physical medicine; increasing importance of chemotherapy; nutrition in relation to disease; changes in nursing service; improved status for the general practitioner; decreasing rates of deaths, infections, and complications; care of chronic and psychiatric patients; advances in professional services; medical staff organization; the professional audit; and the point rating system.

The American College of Surgeons has a fellowship of 15,500 surgeons in the United States, Canada, and other countries. Dr. Irvin Abell of Louisville is Chairman of the Board of Regents. Dr. Malcolm T. MacEachern and Dr. Bowman C. Crowell of Chicago are the associate directors. The College was founded thirty-five years ago. Headquarters are in Chicago.

#### SOUTHERN SOCIETY FOR CLINICAL RESEARCH

A meeting of the Southern Society for Clinical Research will be held at the Roosevelt Hotel, New Orleans January 27, 1948.

#### AMERICAN HOSPITAL ASSOCIATION

How gifts to hospitals can cost donors less than the apparent amount because of decreased income taxes is explained in a brochure issued by the American Hospital Association.

Charitable donations of up to 15 per cent of adjusted gross income of individuals, and up to five per cent of net taxable corporation incomes are exempt from income tax according to current laws, according to the booklet, "Your Gifts to Hospitals through Taxes."

Hospitals over the country are facing spiraling costs like everybody else," said George Bugbee, executive director of the Association, "but the care of patients can't be pared down as some commercial and personal budgets can.

"You can't go halfway on health. That is why funds for expansion and endowments, especially through the easier tax deduction method, are so important to voluntary, non-profit hospitals today.

From \$185.25 saved on a \$5,000 gift to \$95,000 on a \$250,000 donation, substantial economies can



be made, the Association states. Donations of securities and other properties can result in even greater benefits.

Savings of 38 per cent in gifts from corporations and of up to 86.45 per cent in individual gifts are possible under the present income tax regulations, the booklet points out.

#### STANDARDS RECOMMENDED FOR ADOPTION BY THE PHARMACOPOEIAS OF THE WORLD

At its recent sessions in Geneva, from 13 to 17 October, 1947, the Committee of Experts on the Unification of Pharmacopoeias of the World Health Organization of the United Nations, placed 244 items on its Primary List of medicinal substances. These they believe of sufficient importance for immediate attention and inclusion in a book of "Standards Recommended for Adoption by the Pharmacopoeias of the World". This Primary List will be further submitted for review to authoritative medical groups in a number of countries affiliated with the World Health Organization.

A total of 534 drugs were studied. In addition to the items proposed for inclusion in the Primary List, 89 drugs were placed in a Secondary List. The drugs in this second list were known to have some medicinal value but were believed of lesser importance and their standardization can be deferred until a later date. Among the drugs studied, 201 were dropped from further consideration on the ground that they have become obsolete and find little use in modern medical practice.

Starting with the foundations laid by their predecessor, the Technical Commission of Pharmacopoeial Experts of the Health Organization of the League of Nations, the new Committee, during the course of the recent sessions at Geneva, completed the first drafts of 72 monographs of the drugs selected for the Primary List.

During the next few months drafts of monographs will be prepared by the members of the Committee for all items in the Primary List and these suggested texts will be submitted for review to international experts in pharmacopoeial revision.

Another meeting of the Committee is proposed for early next summer, when it is hoped that the First Edition of a book of Standards will be completed.

The present membership of the Committee of Experts includes: Professor H. Baggesgaard-Rasmussen, Chairman of the Chemical Division of the Danish Pharmacopoeia Commission; Professor L. R. Fahmy, Professor of Pharmacognosy, Faculty of Medicine, Cairo; Professor E. Fullerton Cook, Chairman of the Committee of Revision of the United States Pharmacopoeia; Dr. C. H. Hampshire, Secretary of the British Pharmacopoeia Commission; and Professor R. Hazard, Professor

of Pharmacology and Materia Medica, School of Medicine, Paris. Professor Hazard was prevented by illness from attending the October session. Dr. Hampshire, who had been the Chairman of the former Committee, was elected Chairman of the new Committee.

It is expected that the membership of this Committee will be increased, so that additional countries will be represented, and as wide an international basis as possible, will be provided.

#### LOUISIANA STATE MEDICAL SOCIETY WOMAN'S AUXILIARY

The Woman's Auxiliary desires to express their sincere appreciation to Dr. Talbot, the members of the Journal committee and to Miss Shoemaker, for their fine co-operation in again publishing in the Journal the Year Book of the Auxiliary. The Year Book is a valuable aid to the members, for which we are deeply grateful.

A big bouquet of red roses—verbal ones—goes to Mrs. Edgar Burns for her work in assembling and preparing the material for the Year Book. This was a tedious and exacting task, well done, and which it was necessary to perform during the hot summer months. We especially appreciate the effort put forth by Mrs. Burns.

The President of the Louisiana State Medical Auxiliary, Mrs. James W. Warren, attended the Fall Conference of State presidents, presidents-elect and National officers in Chicago on November 6th and 7th, 1947. Mrs. Warren commented that the conference was very helpful and inspiring.

Mrs. Warren desires to express her appreciation to the various chairmen of standing committees who have sent out such inspiring and helpful letters to parish presidents regarding the work of their departments. Each parish president is urged to see to it that these letters are read in open meetings as this is the only medium through which the chairmen can reach and appeal to the members.

Many of our auxiliaries are going forward on our new project "Preservation of Medical Cultural Items". Shreveport, Monroe and Baton Rouge have had Mr. D. W. Postell, Librarian of the Louisiana State University Medical School at New Orleans, speak before their groups on this subject. It is our plea that the Auxiliaries work actively on this project and turn in whatever material they may have to Mrs. Rhodes J. Spedale, Plaquemine, Chairman of Preservation of Medical Cultural Items.

#### NOTICE

The MID-YEAR EXECUTIVE BOARD MEETING will take place in New Orleans on Thursday, February 26th, 1948 and reports will be due at that time. You will be notified of the time and place about ten days before the meeting.

## BOOK REVIEWS

*A Primer of Cardiology*: By George E. Burch, M. D., F. A. C. P. and Paul Reaser, M. D. Lea & Febiger, Philadelphia, 1947. Pp. 272. Price, \$4.50.

This book contains two hundred fifty seven pages including the appendix. It is divided into five chapters.

The first chapter begins by calling the attention of the student to some of the anatomical facts concerned with the study of heart disease and the importance of the position of the heart in the thorax. There are numerous drawings throughout the book to help the reader understand the descriptions given in the text.

In Chapter II there are seventeen signs given as dependable or pathognomonic signs of heart disease. There is a short discussion of each one. In the complete diagnosis, including the functional and therapeutic classification, the authors follow the nomenclature of the American Heart Association: Heart failure—anginal—congestive. The latter divided into left, right and combined ventricular failure and their associated syndromes are described.

The discussions of the conditions are not extensive but are adequate for the purpose of this book. They are consistent with the views of most modern cardiologists.

At the end of Chapter II there are ten pages devoted to the discussion of edema, pointing out that the mechanism of cardiac edema is not fully understood.

In Chapter III heart sounds and murmurs are discussed and the mechanism of their production is described in the text and by drawings.

Chapter IV is devoted to the common types of heart disease. Heart disease is defined as any disturbance in function that disturbs the patient in any way. This includes cardiac neurosis. There are some who might object to a too literal application of the word disease. It is true that some cases of cardiac neurosis are just as disabled and many of them are harder to treat than those with organic heart disease. One of the most helpful means of handling these cases is to be able to tell them truthfully and emphatically that they have no heart disease as this term is understood by the laity. Names given to conditions by physicians have a way of finding their way into the vocabulary of the lay public and are frequently interpreted differently from that intended by the physician. So it might be best not to encourage the application of the word disease to the various types of cardiac neurosis where there is no evidence of actual disease of the heart.

At the end of Chapter IV there is a discussion of congestive heart failure which is very good and should be of interest to all.

Chapter V deals with the bed-side diagnosis of

cardiac irregularities. The subject is well presented for the purpose of the book. A few minor changes in wording would be of advantage. In the treatment of premature beats it is advised to have the patient sleep longer hours, take frequent naps or rest reclining frequently. This would be well for patients with heart disease but when premature beats are the only findings the patient's activities as a rule should not be restricted. It is stated that if a late diastolic, crescendo murmur is heard auricular fibrillation cannot exist. This is true, however, if the diastolic period is short enough and early diastolic murmur may give the impression of being late and being crescendo also even when auricular fibrillation is present.

There is an appendix of sixteen pages in which the nomenclature and classification of heart disease advised by the New York and American Heart Association is reproduced and tables for heart measurements and cardiac diets are given.

One might feel that a little different arrangement of the subject matter would have been better but the book will fill its purpose well and any one interested in cardiology will find the reading of it interesting and helpful.

J. M. BAMBER, M. D.

*The Foot and Ankle: Their Injuries, Diseases, Deformities and Disabilities*: By Philip Lewin, M. D., F. A. C. S. 3rd ed. thoroughly revised. Philadelphia, Lea & Febiger, 1947, Pp. 847. Price, \$11.00

This 3rd edition of Dr. Lewin's popular book has been enlarged by the addition of 227 pages. There have been few if any deletions, and several illustrations have been added. The additions are primarily the advancements which have been made in the methods of treatment since the last edition. They reflect the changing trends of thought brought about by the experience of orthopedic surgeons in World War II and by the introduction of antibiotics.

The same style with readable and accurate information has been retained. The addition of new material has improved the usefulness of this edition as a reference book for all physicians and surgeons concerned with treating disturbances of the feet or ankles.

R. M. KIMBALL, M. D.

*Handbook of Fractures*: By Duncan Eve, Jr., M. D., F. A. C. S., and Thimble Sharber, A. B., M. D. 3rd ed. St. Louis, C. V. Mosby, 1947. Illus. Pp. 263. Price, \$5.00.

This handbook of fractures has been presented for the benefit of the younger members of the profession and for those who only occasionally undertake the treatment of fractures. This is an extreme-



ly practical book, with the emphasis having been placed on the details of treatment. The illustrations are well done and are adequate in number.

The author has consistently brought out the essential factors in the management of the common fracture problems with the minimum number of words. Furthermore, he has presented in detail a single method of treatment of the common fractures which is conservative, modern, and reliable. This brevity and clarity of the text and illustrations, combined with the author's "seasoned" choice of methods, makes this handbook invaluable to the student, interne, resident, and general practitioner.

R. M. KIMBALL, M. D.

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*Handbook of Communicable Diseases:* By Franklin Henry Top, A. B., M. D., M. P. H., F. A. C. P. 2nd ed. St. Louis, C. V. Mosby, 1947. Pp. 992. Price, \$8.50.

This, the second edition of F. H. Top's *Handbook of Communicable Diseases* is divided, as was the first edition, into three sections. The first section is concerned with general considerations relative to communicable diseases. Infection and immunity are discussed briefly, emphasizing tests for immunity and immunization procedures. Chapters on the management of communicable diseases in the home and in the hospital are included. In the second section specific diseases are discussed in a clear, concise form with the diseases classified according to the portal of entry of the causative agent. The last section presents in table form experiences of the Herman Kiefer Hospital with the common communicable diseases.

Special mention of the two chapters, written by nurses, on the management of communicable diseases in the home and in the hospital is deserved. This edition of Top's book has been much improved by the addition of chapters on fourteen diseases not included in the first edition. These include chapters on coccidioidomycosis, rheumatic fever, primary atypical pneumonia, infectious hepatitis, and infectious mononucleosis. The book is adequately illustrated with photographs in color and in black and white. Though this is not a comprehensive and exhaustive work, it is recommended as a ready reference on the more common communicable diseases.

HARRY V. HERNDON, M. D.

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*Cineplasty:* By Henry H. Kessler, M. D., Ph. D. Springfield, Illinois, Charles C. Thomas, 1947. Pp. 201, 314 illus. Price, \$6.75.

This excellent monograph by Kessler is written with well-founded authority. The subject of cineplastic amputations is a controversial one. Much interest was revived during the past war in the entire problem of amputation and prosthetic de-

vices and again in cineplastic amputations. The scope of this monograph is not limited to cineplastic amputations alone, but considers the entire problem of the amputee, both from the physical and psychological point of view, as well as an extensive chapter on the rehabilitation of all amputees.

The sections on the history of cineplastic procedure, the physiology and anatomy, and the surgical techniques are exceptionally good. Chapter VII, which deals with cineplastic prostheses, probably does not convey the true limitations of the present prostheses which are available for such cases. The chapter on phalangization and the chapter on plastic procedures and amputations, cover the procedure of phalangization of the first metacarpal and the use of rotation osteotomy of the fingers to oppose the thumb. The Krukenberg operation, or split forearm operation designed to furnish prehensil power as well as tactile sensation, is thoroughly discussed and evaluated.

The style in which Dr. Kessler writes is extremely readable, authoritative, and quite terse. The critics of the cineplastic amputation and of Dr. Kessler's work in this field have based their criticisms on the lack of an adequate prosthetic device for the fitting of these patients. This monograph furnishes an extensive amount of material for consideration by all who are interested in amputations and the restoration and the rehabilitation of amputees.

JACK WICKSTROM, M. D.

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*Textbook of Medicine:* By Russell L. Cecil, A. B., M. D., Sc. D., Walsh McDermott, M., and Harold G. Wolff, M. D. 7th ed. Philadelphia, W. B. Saunders Co., 1947. Pp. 1730. Price, \$10.00.

When "Cecil's Medicine" was presented originally 20 years ago, it was recognized to be a most welcome addition to the group of useful texts for students. That it is now presented in its seventh edition is adequate evidence to its continued value and worth as a means of imparting clinical information.

As in the sixth edition, the text is presented in double columns. The liberal use of illustrations, and particularly the inclusion of 18 color photographs, makes the text much more readily understood. The current interest in psychosomatic medicine is reflected in a new chapter on this subject; the resurgence of organic neurology is likewise represented by new articles on hemifacial spasm, on narcolepsy and on diphtheritic polyneuritis; similarly there are several contributions on vitamin deficiencies and excesses not previously covered. Practically all of the other articles have been largely revised.

This book can be recommended to any junior or senior medical student for routine use. It will be

of service to many practitioners who wish a brief discussion of those clinical entities usually regarded as within the domain of internal medicine. While most of the discussions are necessarily dogmatic, differences of opinion are frequently admitted by the insertion of an appropriate foot-note.

The seventh edition will undoubtedly be as well received as its predecessors.

SIDNEY JACOBS, M. D.

#### PUBLICATIONS RECEIVED

F. A. Davis Company, Philadelphia: Textbook of Human Physiology, by William F. Hamilton, Ph. D.

Lea & Febiger, Philadelphia: Diseases of the Nose, Throat and Ear (9th edition), by William Lincoln Ballenger, M. D., F. A. C. S., Howard Charles Ballenger, M. D., F. A. C. S., assisted by John Jacob Ballenger, B. S., M. D.; The Foot and

Ankle (3rd edition), by Philip Lewin, M. D., F. A. C. P., and Paul Reaser, M. D.; Surgical Disorders of the Chest (2nd edition), by J. J. Donaldson, B. S., M. D., F. A. C. S.; Unipolar Lead Electrocardiography, by Emanuel Goldberger, B. S., M. D.

Medical Center Foundation and Fund, Chicago: Ulcer, by Donald Cook, B. A., M. D.

C. V. Mosby Company, St. Louis: Handbook on Fractures, by Duncan Eve, Jr., M. D., F. A. C. S.; Synopsis of Neuropsychiatry (2nd edition), by Lowell S. Selling, M. D., Ph. D., Dr. P. H., F. A. C. P.

Henry Schuman, New York: 400 Years of a Doctor's Life, by George Rosen, M. D. and Beate Caspari-Rosen, M. D.

Charles C. Thomas, Springfield, Illinois: Practical Office Gynecology, by Karl John Karnaky, M. D.



# New Orleans Medical and Surgical Journal

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## SYMPOSIUM: CHEMOTHERAPY AND ANTIBIOTICS\*

### CHEMOTHERAPY AND ANTIBIOTICS

MAXWELL FINLAND, M. D.†  
BOSTON, MASS.

It is obviously not possible to cover all of the important aspects of chemotherapy and antibiotics in this presentation. It will be necessary to limit this discussion to some general principles which may help the physician to understand the problems involved and to orient him with respect to the practical uses of these agents. Certain aspects of special interest will also be considered, particularly with respect to those agents which have had wide clinical use. Many important features of the subject will necessarily have to be omitted or mentioned only very briefly.

#### SULFONAMIDE CHEMOTHERAPY

The first successful use of drugs of this group was based on the demonstration of antistreptococcal activity in the azo dye, prontosil. It was soon shown that the active principle of prontosil was the simple compound, para-aminobenzine sulfonamide which is released from prontosil in the body. This compound, now known as sulfanilamide, has had wide and successful use in the treatment of many infections, particularly those caused by the streptococcus, gonococcus, and meningococcus and also in

urinary tract infection due to the colon bacillus. It is also effective against a large variety of other organisms but usually to a lesser extent. In pneumococcal infections, it often proved lifesaving in the treatment of cases of meningitis due to this organism and also in some cases of pneumonia due to type 3 strains, but it was not highly effective in most pneumococcal pneumonias.



Among the favorable features of sulfanilamide are its great penetrating power and its high solubility. Since it is excreted by the kidneys, either unchanged or in the acetylated form, concentrations up to about one per cent are possible and frequently attained in the urine without local complications except under unusual circumstances. Sulfanilamide, however, has many drawbacks. When compared with its more recent derivatives its activity is much more limited and it produces toxic effects of greater severity and more frequently. Those particularly characteristic of sulfanilamide are the cyanosis which is constant, hemolytic anemia which occurs more frequently with this than with other related compounds, nervous symptoms which may be quite disturbing, and occasionally severe liver damage.

Changes in the structure of sulfanilamide made by the addition on the para-amino group tend to inactivate the drug unless the added groupings split off in the body to release the active compound. Acetylation occurs by conjugation in this position within the body and the acetylated sulfonamides are inactive. The addition of various groupings on the sulfonamide end, however, produces profound changes in the sol-

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ubility, absorption and excretion, toxicity and activity. Compounds of the latter type have proved to be the most successful among the many that have been synthesized and tested. See Fig. 1 below.

<b>SULFANILAMIDE</b> 	→ ACETYL SUCCINYL PHTHALYL	 = MARFANIL
 COOH = PABA	→ PYRIDINE THIAZOLE PYRIMIDINE (DIAZINE) MONOMETHYL " (MERAZINE) DIMETHYL " (METHAZINE)	GUANIDINE PYRAZINE

Sulfapyridine was the first such compound to receive clinical trial. It has greater activity than sulfanilamide against the pneumococcus and also against some other organisms including the staphylococcus. Though it lacked the cyanosis-producing property of sulfanilamide, sulfapyridine produced such marked nausea and vomiting and its low solubility resulted in such frequent occurrence of crystalluria, hematuria and renal colic that it rapidly lost favor in this country, particularly after the appearance of sulfathiazole and later sulfadiazine. Sulfapyridine was used continuously by the British throughout most of the war, perhaps because they had a large supply on hand or because they were the ones who first introduced it.

Sulfathiazole proved to be appreciably more active against the pneumococcus, staphylococcus and coliform organisms and also produced much less nausea and vomiting. Drug fever and rashes, which are probably manifestations of sensitization reactions, were much more frequent with this compound. Sulfathiazole, too, is highly insoluble and, in addition, it is excreted more rapidly than sulfapyridine. As a result, precipitation of the drug occurs all too frequently with resulting complications similar to those that were observed with sulfapyridine. When given intravenously in the form of the sodium salt, particularly in a dehydrated patient, precipitation some-

times occurs directly in the renal tubules giving rise to complete anuria without crystalluria or hematuria. Another result of the rapid excretion is the lower blood levels which result from comparable doses when compared with sulfapyridine and sulfadiazine. In addition, sulfathiazole shows much poorer penetration than sulfanilamide, sulfapyridine and sulfadiazine as indicated by the relatively low concentrations of the drug in the cerebrospinal fluid. It has, therefore, not been recommended for use in meningitis, although its greater antibacterial properties and relatively low toxicity make it fully as effective as sulfanilamide and sulfapyridine.

Sulfadiazine, the pyrimidine derivative of sulfanilamide, has proved to be the best compound now available from the point of view of its high antibacterial properties and relatively low toxicity. It is rapidly absorbed, penetrates about as well as sulfapyridine into the cerebrospinal fluid and is excreted more slowly than the previous compounds mentioned. The blood concentrations from the same dose are, therefore, relatively higher. In addition, only a relatively small proportion is bound to serum protein and the acetylated compound is rapidly excreted so that the proportion of inactive drug in the circulating blood is low, except in patients who have poor renal function. Sulfadiazine, has, therefore, come to be used more widely than all the other compounds. It has most of the toxic effects common to the others, although it gives no cyanosis, produces hemolytic anemia extremely rarely and nausea and vomiting quite infrequently. Its relatively low solubility, however, does result in urinary tract complications. In common with the other sulfonamides, it produces sensitization reactions that is, fever and rashes, when given continuously for more than five days and occasionally agranulocytosis if given for more than two weeks.

Three compounds closely related to sulfadiazine are of interest as indicating the effect of minor differences in chemical structure. Sulfamerazine, the only one of these three that has been used to any great



extent, is sulfadiazine to which one methyl group has been added in the pyrimidine ring. This compound is still absorbed quite rapidly but its excretion is much more delayed and as a result higher blood levels are maintained. This was considered to be desirable because of the possibility of using less frequent doses and smaller total amounts. Doses of one gram every eight hours were advocated instead of the usual one gram every four hours. The smaller amount, however, proved much less effective in spite of quantitatively similar or even higher blood levels as compared with sulfadiazine. The percentage of the acetylated form of sulfamerazine in the serum is much higher than with sulfadiazine and furthermore, a larger proportion of the free drug is apparently bound to the serum albumin which further limits its activity. As a result, larger doses were necessary than were at first thought adequate and the resulting higher blood levels and slower excretion increased the frequency of toxic effects.

Another compound first introduced by the British and widely used by them toward the end of the war is sulfamethazine which is similar to sulfamerazine except that it has two methyl groups instead of one. This compound is absorbed and excreted much more rapidly but is acetylated to a greater extent than either of its diazine analogues. Consequently, blood levels are much lower with the same dose, and hence larger doses are required for therapy. This in turn results in much more frequent crystalluria and hematuria in spite of the greater solubility of both its free and acetylated forms as compared with the corresponding forms of sulfadiazine and sulfamerazine.

The pyrazine group has a molecular structure identical with pyrimidine except for the position of the nitrogens. Sulfapyrazine is a highly active compound but it is much less soluble than sulfadiazine, more rapidly absorbed and more rapidly excreted and only slightly acetylated. The resulting blood levels are even lower than those obtained with sulfathiazole, and urinary tract

complications due to precipitation are, therefore, more frequent. For this reason this compound has not received wide acclaim, although even with the low levels this drug seems to be as active as any other compound.

Two features of special interest with respect to the use of sulfonamides may be mentioned because they are not widely or fully appreciated. One is concerned with the problem of sensitization and the other with the renal complications.

The development of fever or a rash and occasionally other symptoms during sulfonamide administration usually indicates the development of sensitization and in the majority of individuals this sensitization will persist. Continuation of the therapy aggravates the symptoms and readministration of the same compound at a subsequent date will bring about a recurrence of symptoms and these are often of great severity and may preclude the use of that drug. It has been found, however, that other sulfonamide compounds may then be used either to continue treatment without interruption or for subsequent therapy at a later date in the great majority of cases. Only about 15 percent of persons who develop these reactions to one of the agents will become so sensitized that they will not tolerate any other sulfonamide compound in addition to the one which occasioned the sensitization in the first place.

Thus, a person who develops a rash and fever from sulfadiazine can receive sulfathiazole immediately to continue treatment and the fever and rash will subside or he can be given sulfathiazole at a later date without having any manifestations provided, of course, that he has not previously had sulfathiazole long enough to become sensitized to it as well. In the case of the three compounds, sulfadiazine, sulfamerazine and sulfamethazine, however, there is a reciprocal relationship so that sensitization to one almost always is accompanied by sensitization to all three. Sulfapyrazine, on the other hand, may be given to a person sensitized to sulfadiazine or to one of its methyl derivatives without recurrence of

symptoms, and the reverse is also true. Persons sensitive to sulfapyrazine will tolerate any of the diazine compounds.

The most frequent complications of the sulfanilamide derivatives thus far discussed are related to their low solubility which results in the precipitation of crystals of the free and acetylated forms within the urinary tract, giving rise, in turn, to hematuria and concretions which then produce renal colic and anuria. It has been found that in water or in urine, each of these compounds retains its own solubility irrespective of the presence or of the amount of any of the other sulfonamides in the same solution. Furthermore, the antibacterial action of any combination of sulfonamide drugs was found to be additive. These facts have led to the suggestion that combinations of sulfonamides may be used to advantage in therapy. The same total dose in the form of a combination of different sulfonamides would have the same activity but would be much less likely to produce urinary tract complications than if a single compound were used.

Lehr in New York suggested the use of a combination of sulfadiazine and sulfathiazole and Frisk in Sweden suggested a combination of equal amounts of sulfadiazine, sulfamerazine and sulfathiazole. Because sulfamerazine is excreted more slowly and sulfathiazole more rapidly than sulfadiazine the Frisk combination results in absorption and excretion relationships almost identical to those obtained with sulfadiazine. Flippin and his colleagues used sulfadiazine and sulfamerazine, a combination which has the merit of two compounds which are mutually related as far as sensitization is concerned, leaving the possibility of using sulfathiazole later should a reaction result from the use of that combination. This would not be possible if the combinations suggested by Lehr and Frisk were used because in that event the patient would most likely be sensitized to both the diazine and thiazole derivatives. Possibly the combination of the three pyrimidine compounds, sulfadiazine, sulfamerazine and sulfamethazine might prove even better since

this combination, like Frisk's, is likely to have absorption and excretion relationships similar to those obtained with sulfadiazine.

For use in enteric infections or for reducing the bacterial content of the bowel, it has seemed desirable to have compounds which are poorly absorbed and yet remain active in the bowel or become active by the release of an active component within the bowel contents. Several different compounds have been used. The first was sulfaguanidine which is highly soluble but poorly absorbed from the bowel. This compound has been widely used but it is much less effective as a bacteriostatic than other compounds and is sufficiently absorbed to give most of the common reactions, including those in the urinary tract. The latter are particularly prone to occur in patients with diarrhea or in tropical climates because the drug is often administered to patients who become dehydrated and excrete very little urine.

Other compounds have been made by additions on the para-amino group of sulfathiazole to form succinylsulfathiazole (sulfasuxidine) and phthalylsulfathiazole (sulfathalidine). These compounds are inactive until they are hydrolyzed in the bowel and the free sulfathiazole is released. Only a very small part of the total amount of the drug ingested is broken down in this manner but this occurs mostly low in the bowel where the sulfathiazole is poorly absorbed and therefore is almost entirely available for action on the bowel contents. Since, however, some material may be broken down higher up in the bowel and since some absorption does take place from lower down, the possibility of sensitization to sulfathiazole exists and actually does occur at times.

A similar result is obtained by a compound in which a COOH group is added to the thiazole ring. This group too is released within the bowel so that activity is probably due to the free sulfathiazole. Carboxysulfathiazole, however, is very poorly absorbed and, when taken by mouth, is recoverable almost entirely in the feces. Other changes in the thiazole ring as in the



case of sulfathiadiazole and one of its methyl derivatives result in much more rapid and much more complete absorption and excretion in the urine in humans. These latter compounds though active in reducing the bowel flora in mice proved less useful in this respect in humans but may possibly be effective in the treatment of urinary tract infections. Because of the rapidity with which these compounds are excreted in the urine, however, the use of large doses at any one time must be avoided if crystalluria and renal colic is to be prevented.

It is difficult to leave the subject of sulfonamides without noting the nature of the chemical groups which are involved in the various active derivatives. The most widely accepted theory of the action of chemotherapeutic agents is that they interfere in any of a number of ways with metabolites essential to the growth of bacteria. In the case of sulfonamides it is considered to be an interference with the normal metabolism of para-aminobenzoic acid which has such a marked similarity to the structure of sulfanilamide. The other structures that have served to enhance the activity of sulfanilamide will be recognized as essential parts of the molecules of known vitamins and co-enzymes.

The group of compounds not inhibited by para-aminobenzoic acid need only be mentioned. The amino grouping in these compounds is separated from the benzene ring. Such compounds were first synthesized in Germany during the war and used topically in the treatment of wound infections. They have proved too toxic for systemic use. The type compound is marfanil. These compounds, while they have been studied in this country, have not received wide acceptance because of their toxicity.

The prophylactic use of sulfonamides has received some attention. In this connection it is necessary to distinguish several distinct situations:

1. The use of a single dose or a single short course for protection against a single exposure as in the prophylaxis of gonorrhea or in the preparation for an operation on

the bowel where spillage of bowel contents may be expected.

2. A single dose or a single short course for a large group of persons exposed to a possible epidemic due to a highly susceptible organism as in the case of the mass and simultaneous prophylaxis in a military camp or other large population unit for the purpose of eradicating meningococcal carriers.

3. Continuous treatment with small daily doses for individuals or for small groups of individuals for a specific indication, as in the prevention of hemolytic streptococcal infections in susceptible persons who are subject to recurrences of rheumatic fever.

4. Mass prophylaxis of a large population with the idea of preventing or reducing the general incidence of bacterial infections as in the case of military units during and immediately after mobilization, when epidemics of respiratory infections, including streptococcal infections may be expected to occur with considerable regularity.

The experiences with sulfonamide prophylaxis to date probably justify the following conclusions:

A single dose of one to four drams or a short course for one or two days is probably not harmful except in two circumstances, namely: (1) in persons who have already been sensitized to the same or sometimes to another sulfonamide by virtue of a previous exposure, and (2) in persons with severe renal damage who will retain the drug for long periods even after these small amounts. Such a dose will probably clear up meningococcal carriers temporarily and prevent infection from exposure to, or during the incubation period of meningococcal infections. It may possibly prevent other infections due to highly susceptible strains of gonococcus, meningococcus, or hemolytic streptococcus and will probably reduce the incidence and severity of postoperative peritonitis following bowel surgery.

Continuous prophylaxis may result in sensitization of an appreciable proportion of individuals and agranulocytosis or other serious complications in a small percentage.

These complications may be serious in themselves and usually will preclude the further use of these compounds. This method may also permit the dissemination of sulfonamide-resistant strains while suppressing or eliminating susceptible ones. Whether the resistant strains that spread are those which were originally resistant or strains which were enhanced in their resistance by exposure to the drug within the body is not entirely clear from the evidence to date. Probably either or both of these possibilities may be operative in this instance. Continuous treatment will probably completely eliminate the chance of the recipient's acquiring meningococcal infections and will reduce the incidence of bacterial respiratory tract infections in these individuals unless or until sulfonamide-resistant strains make their appearance. Recurrent attacks of rheumatic fever should, therefore, be prevented to some extent by such prophylaxis.

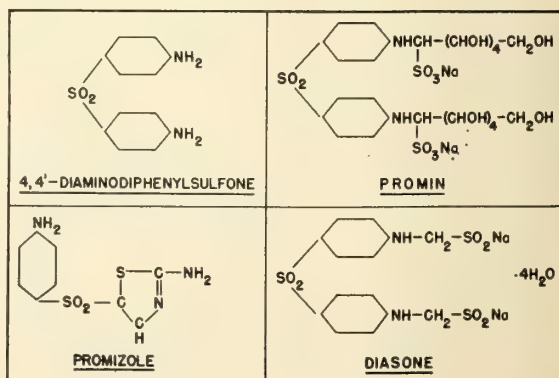
The importance of drug fastness is well demonstrated by the striking increase in the proportion of resistant strains of gonococci during the last few years. At the present time very few susceptible gonococci are encountered whereas resistant strains were quite rare before 1939. The increased incidence of resistant strains of hemolytic streptococci during and after the prophylactic sulfonamide program in some of the armed forces has also been quite striking. Resistant strains of pneumococci have been found to disseminate during continuous sulfonamide prophylaxis against respiratory infections and such resistant pneumococci and hemolytic streptococci may cause serious infections which will resist therapy with any of the sulfonamides.

The evidence to date would indicate that natural resistance to sulfonamides or fastness acquired by exposure of bacteria to sulfonamides within the body is a permanent property of the organism and is not lost on passage. The virulence of strains that are resistant under these conditions is not reduced. This is in contrast to the course of certain organisms which are made resistant to sulfonamides by exposure to these drugs *in vitro*; such organisms may lose

their virulence in the process of acquiring resistance and they may regain their susceptibility when freed from exposure to the drug for a number of generations.

It is worth pointing out that resistance to one of the sulfonamides is accompanied by similar resistance to others when allowance is made for the different degrees of the underlying bacteriostatic action of the different compounds against the particular organism concerned. This is in contrast to what has already been noted in the case of sensitization. Sulfonamide resistance, however, whether natural or acquired does not alter the susceptibility of the organisms to other types of chemical agents and to the various antibiotics.

Brief mention may be made here of the use of chemotherapy in tuberculosis. The sulfonamides are capable of suppressing the growth of *Mycobacterium tuberculosis* in synthetic media and they have a slightly favorable influence on the lesions produced by virulent human strains in a standard type of infection in the susceptible guinea pig. The latter effect, however, has not been very significant. Several compounds, however, have proved effective in such experimental infections. One of them is 4,4'-diaminodiphenylsulfone and two others are derivatives of this compound, namely promin and diasone. A fourth compound, promizole, has also proved highly effective in guinea pigs. The latter compound is very similar in structure to sulfathiazole from which it differs only by the position of one  $\text{NH}_2$  group. The formulas of these compounds are shown in Fig. 2 below. In human





cases the use of all of these compounds has been sharply limited chiefly because of their considerable toxicity. The use of effective doses for long enough periods to bring about favorable results comparable to those observed in guinea pigs has not yet been possible in large numbers of cases. The results, however, are encouraging enough to continue the search along similar lines. The possibility of using these compounds, or similar ones in conjunction with streptomycin or other substances that may become available also requires further and careful study since there is evidence to suggest that such a combination may be helpful and feasible.

Having mentioned the sulfones it seems appropriate also to note the use of para-aminobenzoic acid in the treatment of rickettsial infections. This substance is effective in experimental infections, particularly in chick embryos, but also to some extent in mice. It is excreted very rapidly in the latter and in humans and for that reason frequent and large doses are required to maintain any appreciable concentration in the blood and tissues. With the use of the sodium salt in large and frequent doses, favorable results have been reported in cases of epidemic typhus and possibly in Rocky Mountain spotted fever and in scrub typhus.

#### PENICILLIN

The virtues and properties of penicillin as an antibiotic agent are now well known. Its effectiveness against most gram-positive organisms is appreciably superior to that of the sulfonamides. It is far more effective than the latter in gonococcal infections and is equally effective against sulfonamide-resistant strains as against those which are sulfonamide sensitive. For that reason penicillin has essentially replaced the sulfonamides in the treatment of gonococcal infections. The closely related meningococci, however, are considerably less sensitive to penicillin and much more sensitive to the sulfonamides, and sulfonamide-resistant strains of meningococci have not been encountered. The sulfonamides, therefore, continue to be the drugs of choice in the

treatment of meningococcal meningitis and other meningococcal infections.

Penicillin is not effective against most of the gram-negative bacilli. Occasional strains may be sufficiently susceptible so that local therapy using high concentrations may be successful. Thus occasional cases of *H. influenzae* meningitis and of gram-negative bacillus empyema have been cured by the use of penicillin given respectively by the intrathecal and intrapleural routes in addition to the systemic administration.

Penicillin is highly effective against many spirochetal infections. When used locally or systemically it produces dramatic results in cases of fusospirochetal infection of the mouth. Systemic treatment is highly effective in yaws and in relapsing fever. The results in Weil's disease are variable. When used in large enough doses given over a long enough period, it has produced a high percentage of cures in syphilis. The optimum dose and duration of therapy have not been entirely worked out. Combined therapy with arsenic and bismuth has proved superior to the use of penicillin alone and probably constitutes the most reliable form of therapy at present. While recent work indicates that experimental syphilitic infections in the rabbit may be prevented by relatively small doses of penicillin G, there is at present no evidence to support the hope that similar results may be expected in humans. Syphilis has developed in patients who have been successfully treated with small doses of penicillin for gonococcal infections. In such cases the appearance of the primary luetic lesion may be delayed or prevented, but serological and clinical evidence of the disease appears later.

All of these features of the antiluetic action are independent of the changing character of penicillin which caused much concern not so long ago. The lots of penicillin now available are essentially devoid of the relatively inactive penicillin K and consist almost entirely of penicillin G which seems to be the most effective form available at present. Whether other forms of penicillin or other antibiotics from the same

or other molds will have greater antisyphilitic action remains to be seen.

Penicillin does not appear in significant concentrations in the cerebrospinal fluid after parenteral injection and for that reason intrathecal injections must be used to supplement parenteral injections in the treatment of meningitis. Furthermore the sulfonamide drugs because of their great penetration and their different mode of action are highly useful as an adjunct to penicillin in such cases.

The sulfonamides are inhibited by pus and by the products of tissue break-down. For that reason the local instillation of sulfonamides into suppurative foci has not usually proved of any great advantage. Penicillin, on the other hand, can be used very effectively by local application or instillation into areas of suppuration. It has proved particularly effective when used in this manner in the treatment of serous sac infections, namely in empyema, purulent arthritis and pericarditis. In such cases repeated aspirations followed by instillations of penicillin in generous amounts have resulted in a large proportion of cures without resort to operations. At the Boston City Hospital almost all cases of post-pneumonia empyema due to penicillin-susceptible strains have been successfully treated in this manner during the past two years and the usual mutilating operations have not been found necessary. As much as 200,000 units is injected daily into the empyema cavity in a volume of 10 to 100 c.c. of saline. Lavage of the cavity before each instillation has proved advantageous particularly when the fluid is thick and contains much fibrin. When large doses are given intrapleurally, additional penicillin by intramuscular injection is usually unnecessary because the absorption from the cavity is slow, and significant blood levels of penicillin are often sustained for 24 hours, or even longer. Aspirations and intrapleural injections are continued as long as improvement continues and until a few days after the infection has definitely been controlled as evidenced by all clinical and laboratory criteria.

In osteomyelitis, particularly in the acute

forms but also in chronic cases after the lesion has been freed of sequestra by operative procedures, the prolonged use of large doses of penicillin has brought about consistently good results. The best results follow prolonged and intensive treatment and avoidance of operation as long as clinical and laboratory findings indicate that the infection is controlled and in spite of apparent progression of the lesion in x-rays. The eventual return of the bony structure to normal usually occurs in such cases. Penicillin resistant strains sometimes appear but the degree of resistance is not marked and improvement often continues in spite of the presence of such organisms. In the early postoperative stages in chronic cases, instillations of penicillin through small catheters inserted into the wound have proved helpful.

In subacute bacterial endocarditis due to susceptible organisms the keynote is the same, namely prolonged and intensive treatment. A minimum of four weeks of treatment after the temperature has returned to normal should be insisted on in such cases. The tendency now is to use massive doses but the majority of cases will not require more than a total of 500,000 units a day given in six or eight doses. Only occasional cases due to relatively resistant strains may require larger amounts. The development of resistant strains during treatment has not been frequent and the degree of enhanced resistance has been minor. Occasionally cases which apparently fail to respond to small doses may respond to doses of several million units per day. Others will respond to penicillin X or to streptomycin when they failed to respond to penicillin G but these cases are rare.

The problem of dosage now is considerably different from what it was when penicillin was scarce and very expensive. The general tendency has been to use much larger amounts than are indicated from the sensitivities of the infecting organism and also from the known results in large numbers of cases. There is, of course, no serious objection to such usage, except that it is usually unnecessary, extravagant and



wasteful. One aspect that has interested us is the use of large individual doses in aqueous solutions and the possibility of thereby increasing the interval between injections and reducing the number of injections. The penicillin that is now available gives very little local reactions and can be used in high concentrations so that large amounts may be injected in small volumes without much local irritation. It has been possible to effect cures in most cases of pneumococcal pneumonia with 100,000 units every eight hours. Though effective levels are not usually maintained in the blood for more than half of the interval between injections the results seem to justify this procedure. Similar adjustments for increasing the dose and prolonging the interval may be adapted to other infections or to severe cases.

Large doses of penicillin given at frequent intervals, however, may broaden the scope of penicillin activity to include infections with organisms usually considered to be penicillin resistant. This possibility is suggested by the apparently successful use of such dosage in cases of peritonitis. Doses of 100,000 or 200,000 units every two or three hours will limit the spread of such infection and often effect cure even though the gram-negative bacilli and enterococci usually found in these cases are not very susceptible to penicillin *in vitro*.

Various methods are available for prolonging penicillin action by delaying its excretion and some of these methods have received wide use. The one now most popular is the preparation of penicillin in a mixture of 4.8 per cent beeswax in peanut oil. While it has been widely claimed that a single dose of 300,000 units in such a mixture will maintain effective blood levels in adults throughout a 24 hour period, this has not proved true in the majority of cases. Indeed, blood levels after 12 hours are very erratic, and only a small proportion of patients still have measurable amounts circulating after 18 hours. The preparations have another disadvantage in that they are often difficult to give, especially if vials containing more than a single dose are

used; the local reactions are sometimes moderate or severe and persist for a long time, and sensitization reactions are more frequent from their use than after simple aqueous preparations. New preparations in which the same ingredients are prepared so that they flow freely at room temperature are probably not quite so effective from the point of view of sustaining levels though they are much more convenient to administer. In some sick patients as much as 600,000 units twice a day may be necessary to obtain results similar to those ordinarily observed with 30,000 units of aqueous preparations given every three hours. Preparations containing less than 4.8 per cent beeswax, or none at all as in the products depending on water-in-oil emulsions, have produced too little prolongation of levels to warrant the effort and expense. Far better results are obtained by a substantial increase in the dose of penicillin.

Other agents have been used which prolong the action of penicillin by interfering with its tubular excretion. Diodrast was the first one to be used experimentally. Para-aminohippuric acid also has this effect, but it must be used intravenously in large amounts. Sodium benzoate and restriction of fluid intake have been found useful for this purpose by some workers. Recently a new compound called caronamide has been found to have a similar effect but large and frequent oral doses of this compound are necessary. The details of its practical use remain to be worked out particularly with respect to the possibility of enhancing the action of penicillin taken orally.

Penicillin given orally in simple aqueous solutions produces measurable blood levels fairly constantly if given on an empty stomach, but four or five times as much is required on the average to produce results comparable to those obtained after intramuscular administration. The gastric acidity and motility, inactivation by intestinal bacteria and possibly adsorption on food are all variable factors which may interfere with the proper absorption of oral penicillin. The absorption after meals is extremely erratic and usually unpredictable. Some

persons will obtain no measurable levels even from large doses and the amount recovered in the urine may vary from 2 to 35 per cent of the administered dose. Buffered penicillin tablets are preferable when given after meals and seem to give more consistent results. There seems to be no significant or consistent difference among the various types of buffers. Sodium citrate has been used most frequently but it may occasionally give nausea especially in children. Capsules or coated tablets are undesirable because the site of their disintegration varies in different individuals and the absorption will be minimal if that disintegration takes place below the duodenum.

Simple and uncomplicated infections with susceptible organisms such as acute gonorrhea, pneumococcal pneumonia and streptococcal pharyngitis will respond to oral penicillin if the dose is large enough and given frequently but not within one and a half or two hours after a meal. Oral penicillin, however, cannot be relied upon in the severer infections, particularly those with less sensitive organisms such as the staphylococci.

Penicillin may also be given as an aerosol and this method is being widely used in the treatment of suppurative diseases of the lungs and bronchi. Aqueous solutions of as much as 100,000 units per c.c. and probably even more concentrated solutions of the crystalline penicillin that is now available can be given without local irritation. High penicillin concentrations are thus attained locally wherever the mist penetrates and perhaps up to 25 per cent of the inhaled material is absorbed into the blood and recoverable in the urine. The peak levels in the blood occur early, and demonstrable amounts are found for only short periods, usually one or two hours. The results in certain cases of putrid lung abscess and in diffuse bronchiectasis are quite striking if such treatment is given four to eight times a day for a period of four weeks or longer. In patients who produce large volumes of sputum postural drainage preceding each inhalation considerably enhances the effi-

cacy of the treatment. It may also be used with benefit before operations on the lungs.

Penicillin in large doses has been found effective in the treatment of experimental infections with certain rickettsiae and with some strains of the lymphogranuloma venereum-psittacosis group of viruses. The virus of lymphogranuloma venereum and the immunologically related viruses of trachoma and inclusion blennorrhea, are also susceptible to sulfonamide drugs but most of the psittacosis group are not. Of local interest is the fact that the strains of the psittacosis-like virus that were responsible for the recent outbreaks of pneumonitis in Louisiana and California and which produced such a high mortality are among the ones that have shown definite though not marked susceptibility to penicillin. The results of treatment of infections with these agents in humans have not been very striking though there is no wide experience and possibly the doses used have not been adequate.

The prophylactic use of penicillin has not received attention in the past but may be widely applied in the near future. One or more injections of 50,000 or 100,000 units just before and after tooth extractions or other dental manipulations in patients with rheumatic or congenital heart disease may minimize the chances of developing bacterial endocarditis. The use of penicillin (and sulfonamides, too) during severe influenza virus infections or in cases of extensive viral pneumonia may also prove useful in preventing the occurrence or spread of the highly fatal bacterial complications. The use of penicillin in the prophylaxis of venereal infections is an obvious corollary to its use in the treatment of these diseases, but no reliable data on the effectiveness of such prophylaxis is now available. The possible complications of its widespread use and particularly the potentialities for producing or disseminating resistant strains are virtually unknown.

#### STREPTOMYCIN

Streptomycin was the product of a systematic study undertaken deliberately in an attempt to discover antibiotics which are



effective against the gram-negative bacilli and the mycobacteria, since most infections with these organisms proved not to be highly susceptible to penicillin and to the available chemicals. When it was first discovered and found to be active against both of these groups of organisms, it was hoped that streptomycin would provide the missing link in the conquest of the bacterial diseases. This hope has not been entirely fulfilled. Nevertheless, streptomycin has proved quite useful although when compared with penicillin, both from the point of view of activity and toxicity, it is quite disappointing.

It is well to bear in mind from the very start the relative effectiveness of penicillin and streptomycin. This is indicated in the very definition of their units, the sensitivity of various strains, the range of dosage that has been found effective and the limits of tolerance. The unit of penicillin was originally defined as that amount which completely inhibits the growth of 50 c.c. of a standard staphylococcal culture. It is now defined by weight as the equivalent of 0.6 microgram of pure crystalline penicillin G. Most strains of gonococcus and hemolytic streptococcus are sensitive *in vitro* to between 0.01 and 0.04 unit or the equivalent of 0.006 and 0.024 microgram. Most staphylococci are sensitive to concentrations between 0.02 and 0.2 unit, that is, between 0.012 and 0.12 microgram. Most cases of acute gonococcal urethritis will be cured by a total of 100,000 units, or 60 milligrams of penicillin G. A case of pneumococcal pneumonia will require a total of between 300,000 and 500,000 units or 180 to 300 milligrams of penicillin. Larger doses than these are now widely used but they are not necessary and are given only because that can be done without danger. Indeed, the maximum tolerated dose of penicillin in humans is virtually unknown.

The unit of streptomycin was originally defined as that amount which will inhibit the growth of 1 c.c. of a culture of *E. coli*. It is now defined as one microgram of pure streptomycin base. Very few gram-negative bacilli are sensitive to less than 1 unit and

most of the so-called sensitive strains require between 3 and 15 units. Doses of streptomycin are usually given in grams and the average adult receives between two and six grams a day for most of the susceptible infections. These amounts probably approach the minimum effective dose and nevertheless will be more than ten times the usual dose of penicillin by weight. Furthermore, the maximum tolerated dose of streptomycin is not much more than twice this amount. The cost per million units in sterile vials is very nearly the same for the two agents.

Streptomycin is, nevertheless, a valuable addition to the group of agents which are used for the definitive treatment of infectious diseases, particularly since it is effective in a number of infections which are benefitted little if at all by other available agents. Streptomycin has proved most effective in cases of acute tularemia. It has also produced cures in a large percentage of cases of meningitis due to gram-negative bacilli particularly *H. influenzae*. It is useful in many other gram-negative bacillus infections particularly those of the urinary and respiratory tracts. Typhoid fever, Salmonella infections and brucellosis, however, have not responded favorably. In certain cases of coccal infections which have failed clinically to respond to sulfonamides and penicillin or in which organisms were resistant to these agents, streptomycin has proved useful as a second line of defense.

The present consensus in regard to the role of streptomycin in the treatment of human tuberculosis is that it exerts a palliative effect by producing some degree of bacteriostasis. Most patients who have active infection with fever show decided clinical improvement within the first two weeks after treatment is started. The immediate results generally have been most striking in the miliary, meningeal and laryngeal forms of tuberculosis. The meningeal form is not benefitted unless the drug is given intrathecally as well as intramuscularly. The disease requires large doses, probably a minimum of two to three grams a day in adults for prolonged periods. Treatment

should not be undertaken unless adequate amounts of streptomycin are available to permit continuous therapy for at least three to four months. The development of resistant strains has been very frequent and has limited the effectiveness of this agent. It is generally agreed that streptomycin cannot be regarded as a substitute for present methods of sanatorium and surgical therapy.

From the point of view of the community as a whole it is probably wise, for the present, to limit the use of streptomycin in tuberculosis to the few clinics where carefully controlled and prolonged treatment and study is possible. Only on the basis of the results in such controlled groups of cases may one expect to determine the real and permanent value of streptomycin in the various forms of tuberculosis. The results of such studies carried on over a sufficiently long period may clarify the limits of usefulness and the best method of employing streptomycin both in individual cases and in groups of cases. The possibility of the use of combinations of streptomycin with the sulfone drugs also requires extensive study before any general program is suggested.

It is important to emphasize that general hospitals, particularly with the crowded conditions now prevalent, are not equipped to handle this problem and should not be expected to do so. It is still too soon to recommend any long range program even for the specialized institutions. In the meantime, it is hoped that better, more effective, less expensive and less toxic agents will become available. In particular, it is hoped that some effective agent will be discovered with which the development of resistance will not be such a prominent feature.

In the treatment of the urinary tract infections due to gram-negative bacilli the most important limiting factors from the point of view of streptomycin therapy has been the rapid development of extreme degrees of resistance in the organisms during the course of treatment. These resistant organisms persist once they appear and, as a result, the infections either fail to im-

prove or relapse. Increases in the dose of streptomycin fail to prevent the appearance of resistant strains in spite of the fact that levels are maintained in the blood which are higher than those required by the *in vitro* sensitivity of the strains. Of course most of the patients in whom streptomycin has been used have had chronic infections with associated structural defects which interfered with successful therapy and predisposed to recurrence of infection in those who were apparently improved.

It has been shown that streptomycin is considerably more effective *in vitro* in an alkaline than in an acid medium. In the cases which were studied at the Boston City Hospital, it was noted that in those patients in whom failure to respond to streptomycin was associated with the development of resistant strains, the urine had been acid before treatment was started and throughout the course of streptomycin therapy. An attempt, therefore, was made to determine the effect of alkalis on the urine in such cases. In most instances sodium bicarbonate and potassium citrate usually six grams of each a day in four or six divided doses were given in an attempt to maintain a pH of 7.5 in the urine throughout the period of therapy. In some cases as much as ten grams of each of these alkalis were required to obtain this result. On this regime most patients showed a good bacteriological and clinical response to streptomycin and resistant strains were encountered much less frequently.

The results in certain cases of meningitis have been particularly noteworthy. Streptomycin alone has proved more effective than the combination of specific antiserum and sulfadiazine in cases of *H. influenzae* meningitis. We have had only one death in 16 consecutive cases and the majority of these patients were under one year of age and had positive blood cultures before streptomycin treatment was started. Many of them had previously failed to respond to treatment with penicillin and sulfadiazine and some of those due to type b strains had also received specific antiserum.

Although there is some penetration of



streptomycin from the blood stream into the cerebrospinal fluid, especially in cases of meningitis, the concentrations are quite low. Cases have been reported in which meningitis has developed during the course of treatment with streptomycin. For these reasons streptomycin treatment of meningitis whether due to gram-negative bacilli or to *Mycobacterium tuberculosis* must include both intrathecal and intramuscular injections. Intrathecal doses of 50 to 100 milligrams in a volume of 5 to 10 c.c. of cerebrospinal fluid or saline have been given every 12 to 24 hours in adults. In infants injections of 25 to 50 milligrams have been given intraspinally and 25 milligrams have been injected into the ventricles through the fontanelles and seem to be well tolerated.

Cures have been obtained in the majority of cases of meningitis due to various gram-negative bacilli other than *H. influenzae* and we have observed one instance of apparent recovery in a case of tuberculous meningitis. Similar results have been obtained by others. In the cases of meningitis the effectiveness of streptomycin was readily apparent by the rapid disappearance of organisms first from the smears and then from cultures of cerebrospinal fluid. Blood cultures usually become negative after the first intramuscular dose. The sugar content of the spinal fluid rises rapidly. The cell count and the protein content of the spinal fluid drops progressively and the percentage of polynuclears drops and this is accompanied by a corresponding increase in the proportion of lymphocytes. Almost all of the patients with meningitis that have been treated with streptomycin have had a drop in their temperature and marked clinical improvement in from one to four days. Fever often recurs and then persists until the streptomycin is discontinued. Resistant strains have not been encountered in any of the cases of meningitis due to *H. influenzae* that we have studied although this has been observed in a number of cases by others. We have observed the development of resistance during treatment in a case of meningitis, due to *Pseudomonas aeruginosa*.

In the cases of respiratory tract infections streptomycin has been used by intramuscular injection or as an aerosol. The latter has been reserved mostly for the chronic suppurative types of infection and the usual dose has been from 100 to 200 milligrams in 1 or 1.5 c.c. of distilled water. These aerosol treatments are given four to eight times a day. Resistant strains have developed in a case in which the streptomycin was given only by aerosol, but they have appeared after intramuscular injections alone or after combined therapy. In one case in which streptomycin and penicillin were used in succession Friedländer bacilli and pneumococci both became resistant during streptomycin treatment but neither of these organisms became resistant to penicillin given in smaller doses over a similar period in spite of the fact that these organisms persisted throughout the entire course of treatment.

The results of streptomycin treatment in pulmonary infections have varied and here again the appearance of resistant strains appeared to be the greatest limiting factor. In cases of chronic respiratory infections the underlying pathology is not altered but the infection may be limited or halted and healing promoted so that at least the progression of the disease may be arrested.

Streptomycin is not absorbed from the bowel. When given by mouth it reduces the fecal flora markedly. Oral streptomycin has, therefore, been used successfully in preparation for large bowel surgery and in the treatment of bacillary dysentery.

The toxic effects of streptomycin have not been very frequent except in patients who received large doses over prolonged periods. The local reactions from intramuscular injection include pain, tenderness and induration at the site of the injections, often accompanied by local redness and heat. They are more severe after subcutaneous injection and may be somewhat reduced by incorporating procain in the injection. Occasionally these reactions are followed by generalized muscular pains and malaise. Intrathecal injections sometimes give an increase in pleocytosis at first and if the dose

is too large there may be an increase in pressure. Earlier and probably impure lots gave more serious complications but these are no longer encountered.

The most common constitutional reaction is a histamine-like effect consisting of headache, flushing of the skin, nausea, vomiting, fall in blood pressure and occasionally convulsions. These were more frequent with the early impure lots and are rarely encountered after intramuscular injections at present but may be observed if the streptomycin is given intravenously at too rapid a rate. These reactions may apparently be avoided by the use of benadryl and possibly with pyribenzamine. Skin eruptions and fever may appear and these may take on various forms including exfoliative dermatitis and they may recur on subsequent administration of streptomycin. Streptomycin should usually be discontinued when these reactions appear.

The most striking and most disturbing toxic effect of streptomycin has been the changes in vestibular function and this apparently is a property of streptomycin itself and not of any of its impurities. The incidence of this reaction in humans varies but recent reports indicate that up to 90 per cent of persons receiving streptomycin in the treatment of tuberculosis may be affected. Patients may complain first of dizziness, light headedness, or giddiness, particularly when they change position. The loss of vestibular response as judged by a positive Romberg test and by the response to the caloric and rotation tests has persisted in most of the patients in whom treatment was continued for some time after the symptoms began. Patients may compensate, however, for this defect by other postural mechanisms so that the symptoms will usually persist and be incapacitating for only one to three months. Other toxic effects are minimal. The other serious sequellae which have been observed in patients who have recovered after treatment for tuberculous meningitis and occasionally other forms of meningitis are probably the effects of the meningitis rather

than the toxic effects of the drug in most instances.

#### CONCLUSION

It seems proper to emphasize one point which is not fully appreciated nowadays. Throughout this presentation references were made to specific types of bacteria, to sensitivity of different strains and to blood levels of the antibacterial agents. All of these features of antibacterial therapy must be interpreted as indicating that laboratory control is still an important and essential part of the intelligent and proper management of infectious diseases. The extent to which laboratory methods are used will vary, of course, with the particular needs and the available facilities. It would be unfortunate indeed if the wide effectiveness of these chemicals and antibiotics were interpreted as indicating that laboratory diagnosis and follow-up are no longer needed in the conduct of cases of bacterial infection. The specific aspects of the use of the agents that have been discussed should indicate quite forcefully that the reverse is true.

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### THE SURGICAL USE OF CHEMOTHERAPEUTIC AND ANTIBIOTIC AGENTS

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NEW ORLEANS

The surgical specialists of today are probably more skeptical than any other group of the therapeutic advantages of presently available antibacterial therapy. It is only natural that this should be so. The prerogative of treating infections responding solely to antibacterial agents has been usurped by the internist and general practitioner. The surgeon is consulted only when the infection is clinically persistent in spite of adequate chemotherapy or antibiotic therapy. Under such conditions it is usually possible for the surgeon to find an abscess, a focus of necrotic tissue, or an infected thrombus requiring surgical treatment. An important consequence of this clinical trend of altered responsibility is the development of funda-

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mentally different philosophies regarding antibacterial therapy by the surgical and non-surgical specialists. The internist and general practitioner look upon antibacterial therapy as a measure of primary importance, whereas the surgeon relegates it to an adjuvant position. Unquestionably, many infections are adequately treated solely by the administration of the proper antibacterial drug. By the same token many infections could be more effectively treated by surgical means alone. Hence, as is always true in conflicting philosophies, there is some question as to the relative value of the various antibacterial agents.

Even among surgeons there has been considerable controversy as to the merits of systemic chemotherapy as compared with topical applications. Again the source of the debate is to be found in a differing point of view. On the one hand, there were those concerned primarily with sterilization of the wound and disappearance of bacteria in the smear and culture. The other group sought to obtain healing of the wound regardless of its bacterial population. Both were motivated by a fundamental instinct of human nature—a desire to do something directly to the wound. At the moment the controversy seems to have been settled by the surgical experience of World War II. It has been established that local chemotherapy is not only unnecessary but frequently undesirable. Under the protection of systemically administered antibacterial agents, debridement of both recent and infected wounds has been shown to be practical and safe. In other words, the instinctive urge to treat the wound has been directed toward early closure instead of toward bacterial sterilization of the wound.

Clinical experience has justified the creation of two separate categories of surgical infection: invasive infection and wound suppuration. The surgically important and frequent types of invasive infection are those due to the hemolytic *Streptococcus*, *Staphylococcus*, and toxigenic *Clostridium*s. Suppuration of wounds is usually due to a mixed or polybacterial infection. Although the organisms responsible for invasive in-

fection may be found in wound suppuration, they are rarely acting in their capacity as invasive pathogens. Furthermore, wound suppuration is not dependent upon the presence of potentially invasive pathogens. The organisms important in wound suppuration are proteolytic. The most frequently encountered types of proteolytic bacteria are *Bacillus proteus*, *Pseudomonas* (pyocyaneus) and *Clostridium sporogenes*. These organisms either are initially resistant or rapidly acquire resistance to presently available chemotherapeutic agents. Since they lack invasive attributes, their presence in the wound is dependent upon the availability of a pabulum of devitalized tissue or exudate protein. An important observation during the recent war was recognition that a blood clot was as acceptable as devitalized muscle for the growth of anaerobic bacteria. From these observations it has been concluded that the best means of treating wound suppuration is to rid the wound surgically of devitalized tissue and blood clot. The great surgical advantage of antibacterial therapy in wound management lies in the capacity of these drugs to protect living tissue from further destruction by invasive bacteria during periods of surgical manipulation. If the objective of chemotherapy is recognized as the protection of living tissues from the hazard of invasive infection, then the systemic route is the desirable method of treatment. Within such a concept of management of open wounds there is no place for topical applications of antibacterial agents.

It is pertinent at this time to comment upon another controversial matter. Some internists still advocate the intrapleural injection of chemotherapeutic or antibiotic agents in the management of empyema. Most surgeons have abandoned this practice. It is practical to consider empyema in two phases: the pleural abscess and pleural cellulitis. Even if it is granted that an occasional abscess may be sterilized by the topical instillation of such drugs as penicillin, it must be recognized that non-drainage methods prevent optimal functional rehabilitation of the underlying lung. Bacterial

sterilization of a wound must not take precedence over functional restoration of the affected part. The second type of empyema may be classified as pleural cellulitis with effusion. It is this type of empyema which responds dramatically to repeated aspirations of fluid with injections of antibacterial drugs. It has been my clinical experience that this type of infection responds equally well to continued systemic therapy with repeated pleural aspirations without supplemental local instillations of penicillin. Most of the observations regarding delayed diffusion of antibacterial agents into the pleural or serous cavities refer to the normal and not to the inflamed serous surface. It has been repeatedly demonstrated that in the presence of inflammation there is increased diffusibility of antibacterial agents into the area of inflammation.

Especially important for surgical consideration is the pathogenicity of coliform bacteria. The ease of isolation and the preferential growth of these organisms on artificial media have, in my opinion, unduly emphasized their importance. With the exception of the relatively infrequent paracolon-aerobacter, these bacteria are lacking in invasive and proteolytic characteristics. As such, they are more properly classified as commensal, or saprophytic, bacteria. Their persistence in an infection has been correlated with the presence of the intermediary products of protein break-down. In wounds such products are usually the metabolic by-products of the biologic activity of other organisms. Only in serum, urine, bile, and spinal fluid is there a sufficient metabolic substrate of small molecular nitrogenous compounds to support the survival and growth of these bacteria. In the management of wounds it is usually possible to suppress the exudation of serum by pressure dressings. The control of these organisms presents no specific problem in wound management if exudation is arrested. Specific chemotherapy designed to arrest the survival and growth of coliform bacteria is justified only in the management of infections of the urinary tract,

biliary tract, and cerebrospinal system.

The saprophytic role of coliform bacteria has been established with greatest certainty in the treatment of peritonitis. There is now abundant clinical and experimental evidence to conclude that streptomycin, either alone or as adjuvant antibiotic therapy, fails to alter the course of peritonitis dramatically. On the other hand, penicillin given in dosage as great as 100,000 units every hour, according to the severity of the case, has been sufficiently effective to establish the gram-positive bacteria as the important pathogens in peritonitis. In consequence of clinical experience with the antibacterial therapy of peritonitis, it is possible to draw one further significant conclusion. Even more important than bacterial contamination is the escape of activated digestive enzymes into the free peritoneal cavity. In the surgical treatment of peritonitis, primary attention is directed to excision of necrotic tissue and exteriorization of intestinal fistulas. Once this has been achieved, the peritoneum has an extraordinary capacity to deal with the residual factor of bacterial contamination. Undoubtedly, this is accomplished more expeditiously if penicillin is given in adequate doses, and the clinical results are extremely satisfactory. Certainly there is no need for the routine administration of another antibacterial agent, either a sulfonamide or streptomycin. At the present time it is our practice to give supplemental streptomycin therapy (0.5 gm. every four hours) only to those desperately ill patients in whom the likelihood of fatal issue justifies the use of all conceivably helpful adjuncts to established therapeutics.

The surgeon of today is grateful for the therapeutic advantages offered by presently available drugs. Hemolytic streptococcal and staphylococcal infections are now adequately treated with minimal debility and rapid convalescence. Anaerobic cellulitis and gas gangrene present less formidable problems than previously. The surgeon also looks to the future, and knows what he wants in the way of new antibiotic compounds. Most urgently needed is an agent



for the control of infections produced by *Clostridium sporogenes*, *Pseudomonas* and *Bacillus proteus*. Within present concepts of reparative wound management, the new compound should be effective when given systemically. It is significant to note that none of the currently experimental compounds, including bacitracin, meets these needs. It seems likely that penicillin will remain the antibiotic of choice in surgical treatment for a considerable time to come. Current clinical investigations suggest that immediate advances may be made by continued upward revision of present dosage programs for such resistant infections as peritonitis and bronchopulmonary suppuration. It is known that dosages of 25,000,000 to 40,000,000 units of penicillin per day may be given safely.

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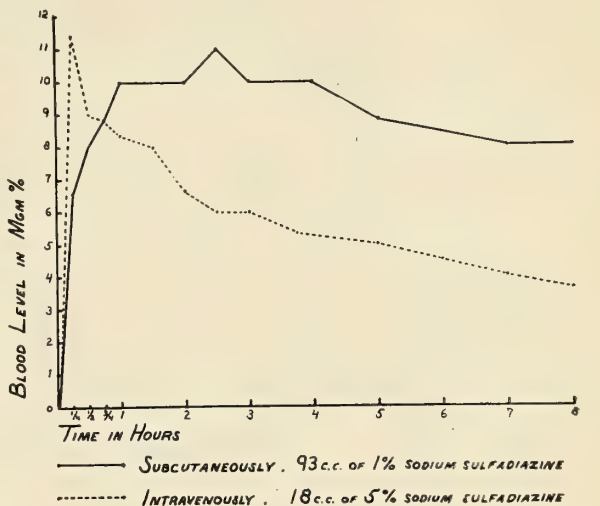
## USE OF ANTIBIOTICS IN PEDIATRICS

GEORGE W. SALMON, M. D.

HOUSTON, TEXAS

I have greatly enjoyed the informative presentations of the preceding speakers. Since they have covered the subject so well and since the time allotted to this symposium is growing short, I shall restrict my remarks to a few case presentations. These are cases that have been seen either by my colleagues or myself in the past few years. They have been selected because they illustrate some particular problem, not because they were handled in an ideal manner or because we are particularly proud of them. Some of these cases have appeared in previous reports. The charts used to illustrate the cases contain only pertinent material—negative tests and procedures being, in general, omitted.

First, I should like to show a chart (see figure 1) which explains why we prefer the subcutaneous to the intravenous route for parenteral administration of sulfonamides. A more even, better maintained level follows subcutaneous administration. One-third of the 24 hour dose should be injected subcutaneously at eight hour intervals. We



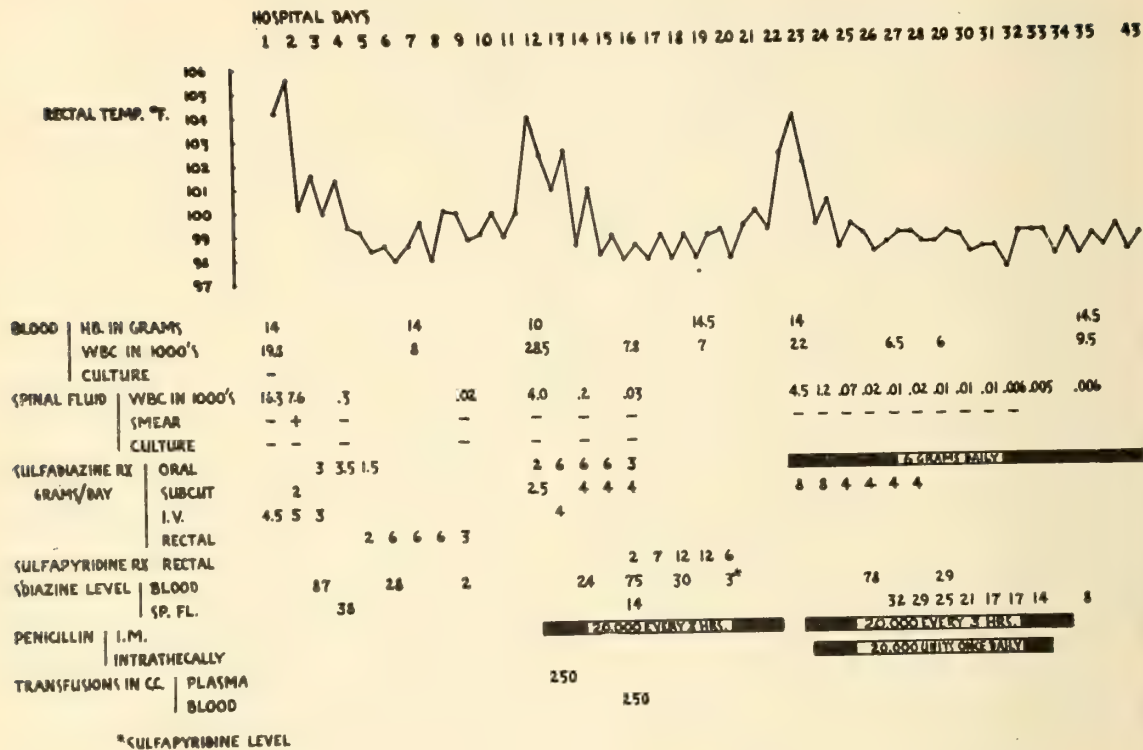
AGE 15 MONTHS : WEIGHT 9.3 KG. : DOSE = 0.1 gm/kg

Fig. 1: Comparison of blood levels to be obtained from the subcutaneous and the intravenous administration of sodium sulfadiazine. Levels as whole blood free sulfadiazine. After several injections higher levels are built up, but this serves to illustrate the type of curve obtained by each method.

usually employ a one or two per cent solution of the sodium salt in saline or lactate-Ringer's. Oral therapy should not be relied on exclusively in severe infections.

We had one patient with pneumococcal meningitis complicating acute mastoiditis. Since this case, as well as some of the others, was seen before the supply of penicillin became plentiful, the doses used seem small when compared with those used in the past year. We have not, however, increased the dose of intrathecal penicillin and still employ 10,000 or 20,000 units dissolved in 10 c.c. of saline once or twice daily.

Figure 2 illustrates a case of pneumococcal meningitis with two relapses. Since the original attack and each of the relapses were treated differently this case actually illustrates three modes of therapy. The original attack was treated with sulfadiazine alone and the response was satisfactory. When the route of administration was changed to rectal the blood level fell to 2 mg. per cent. When the sulfadiazine was discontinued the disease relapsed within 48 hours. The first relapse was treated with sulfadiazine and systemic administration of



CASE R. WHITE MALE AGE 3 YRS. 7 MOS. WEIGHT 40 LBS. CASE NO. 280  
PNEUMOCOCCAL MENINGITIS, NOT TYPED VOMITING AND FEVER OF TWO DAYS DURATION COMATOSE  
SEQUELLA: BILATERAL NERVE DEAFNESS

Fig. 2: See text.

penicillin. However, when the route of administration of the sulfonamide (which had been changed to sulfapyridine) was changed to rectal the blood level fell to 3 mg. per cent. When the sulfonamide was discontinued the second relapse began within 24 hours. This second relapse actually began while the child was receiving 20,000 units of penicillin intramuscularly every three hours. The treatment of the second relapse was different in two respects. This time intrathecal penicillin was administered and the oral administration of sulfadiazine was continued well into the period of convalescence. Among several lessons to be learned from this case are: (a) in treating meningitis, sulfadiazine should be contin-

ued after the patient has made a clinical recovery; (b) the rectal route of administration does not consistently provide a satisfactory blood concentration; (c) intrathecal therapy is essential—this child actually relapsed while receiving intramuscular penicillin.

Figure 3 illustrates an interesting disease, sodoku, the *Spirillum minus* variety of rat-bite fever (the other variety is caused by the *streptobacillus moniliformis*). Sodoku responds readily to penicillin as here demonstrated. Notice that after penicillin was started the lesions became worse. This is a Herxmeimer or flare-up effect; it has also been noted following the treatment of this disease with arsenicals.



## SODOKU

CASE J.P.G.

#84993

COL. O→

AGE 14 YRS.

MAY 2 3 4 5 6 7 8 9 10 11 12 13 14 15



PENICILLIN 10,000 UNITS IM q 3 HRS.

WBC IN MILLIONS	4.4													
HB IN GRAMS	13													
WBC	13,000			6,950				5,400						
GRANULOCYTES	80			58										
WASSERMANN	NEG.								NEG.				NEG.	
EDEMA OF LESIONS	++	++	+++	+++	++	++	+	+	+	-	-	-	-	-

MARKFIELD-LESION ON CHIN \_\_\_\_\_ NEG. SPECIAL CULTURE FOR STR-BAC. MONILIFORMIS-BLOOD \_\_\_\_\_ NEG.  
 MARKFIELD-MATERIAL ASP. FROM LESION ON ARM \_\_\_\_\_ NEG. SP. CUL. FOR STR-BAC. MF-MAT. ASP. FROM LESION ON ARM \_\_\_\_\_ NEG.  
 ROUTINE CULTURE-BLOOD \_\_\_\_\_ NEG. MOUSE INOCULATION FOR SPIRILLUM MINUS-BLOOD \_\_\_\_\_ QUES.  
 ROUTINE CULTURE-MAT. ASP. FROM LESION ON ARM \_\_\_\_\_ NEG. MOUSE INOC. FOR SP. MINUS-MAT. ASP. FROM LESION ON ARM \_\_\_\_\_ POS.

Fig. 3: Sudoku treated with penicillin.

ACUTE SUPPURATIVE ARTHRITIS, RIGHT HIP, STAPHYLOCOCCUS AUREUS

E.F. - AGE 13 MO.

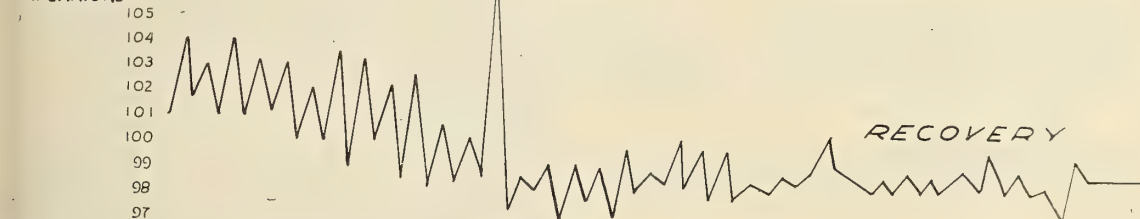
DAY 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 45

R.B.C. AND HB. 37 10 gm 26 7 gm 26 7.5 gm 37 10.5 gm 34 10 gm 47 14 gm

W.B.C. 9000 6000 17000 9300 14000 18000 8700 7100

TRANSFUSION 72 P 77 P 17 P 49 P 71 P 68 P 47 P 30 P

TEMPERATURE 106 105 104 103 102 101 100 99 98 97



PENICILLIN I.M. 80,000 UNITS DAILY

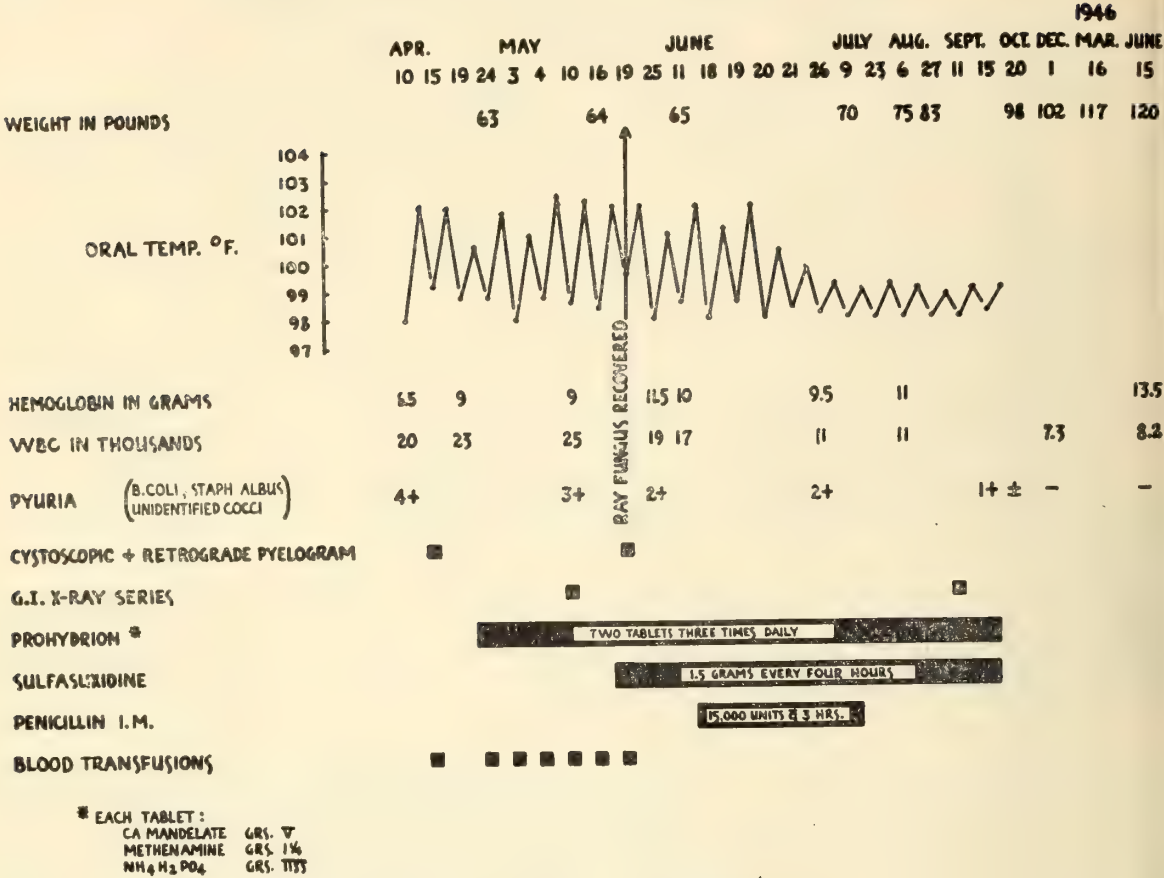
PENICILLIN IN JOINT 25,000 UNITS ONCE DAILY

ASPIRATION OF RIGHT HIP JOINT PUS CL. CL. PUS CL. CL. PUS CL. CL. CL. CL. PUS

CULTURE FROM RIGHT HIP JOINT 4+ 3+ 3+ 1+ 2+ 2+ 1+ 2+ 1+ 3+ 1+ - - - 1+

BLOOD CULTURE - +

Fig. 4: Pyogenic arthritis treated without surgical drainage.



CASE C.W., 15 YR. WHITE ♀, NO. 84531

Fig. 5: Abdominal actinomycosis treated with penicillin.

Figure 4 illustrates a particularly severe case of pyogenic arthritis caused by *Staphylococcus aureus*. It was treated without surgical drainage. Penicillin was given systemically and once daily locally in the hip joint, following aspiration. The rather slow response may be due to the rather small intramuscular doses that were being used when this child was treated. The temperature spike on the thirteenth day was part of a transfusion reaction.

Figure 5 illustrates a case of abdominal actinomycosis. There were fistulae from the intestinal tract to the genito-urinary tract (resulting in a severe pyuria) to the abdominal wall. The temperature record does not attempt to outline her day by day course, but rather selected typical days. Consecutive days are, however, included for a few days immediately following the institution of systemic penicillin therapy.



Fig. 6: Cavernous sinus thrombophlebitis treated with penicillin, sulfadiazine, and anti-coagulants: before treatment.



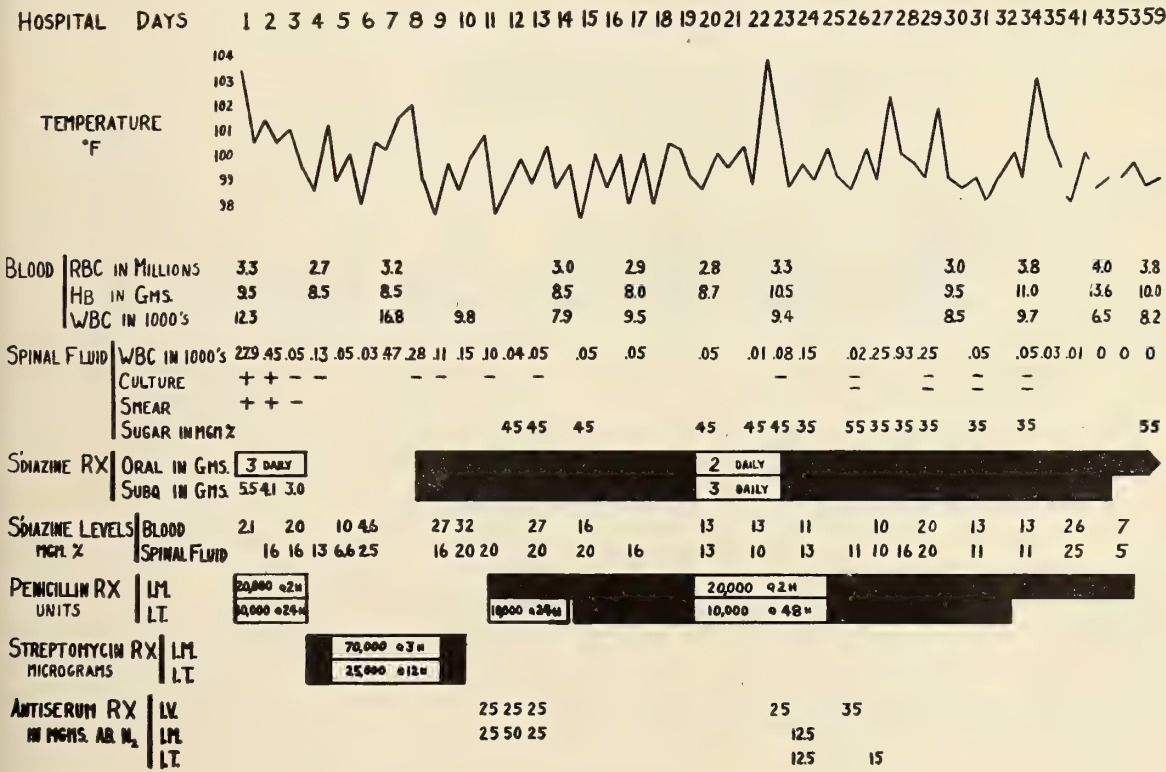
Figure 6 is the photograph of a nine year old boy with a severe case of cavernous sinus thrombophlebitis. The blood culture was repeatedly positive for staphylococcus



Fig. 7: Cavernous sinus thrombophlebitis, after treatment.

albus. The case was treated with penicillin, sulfadiazine, and anticoagulants. Figure 7 is another photograph taken following recovery.

Figure 8 illustrates a case of meningitis due to type B, *Hemophilus influenzae*. It is likely that the penicillin used had little or no effect on the course of the disease. It has been included on the chart for the sake of accuracy, however, since it was used. Note that the infant was responding nicely to sulfadiazine. When streptomycin was obtained (at that time it had to be flown from New York by special request) the sulfadiazine was discontinued. While receiving streptomycin alone (both intramuscularly and intrathecally) the disease relapsed. It is well known now that many cases of influenzal meningitis do not respond to streptomycin. In this disease streptomycin should not be used to the exclusion of other forms of therapy.



CASE D.S. ♀ AGE 8 MOS. WT 22 LBS. HH#93764

Fig. 8: See text.

EMPHYEMA DUE TO UNIDENTIFIED GRAM POS. COCCUS  
CASE T.W. #82755 AGE 20 MOS.

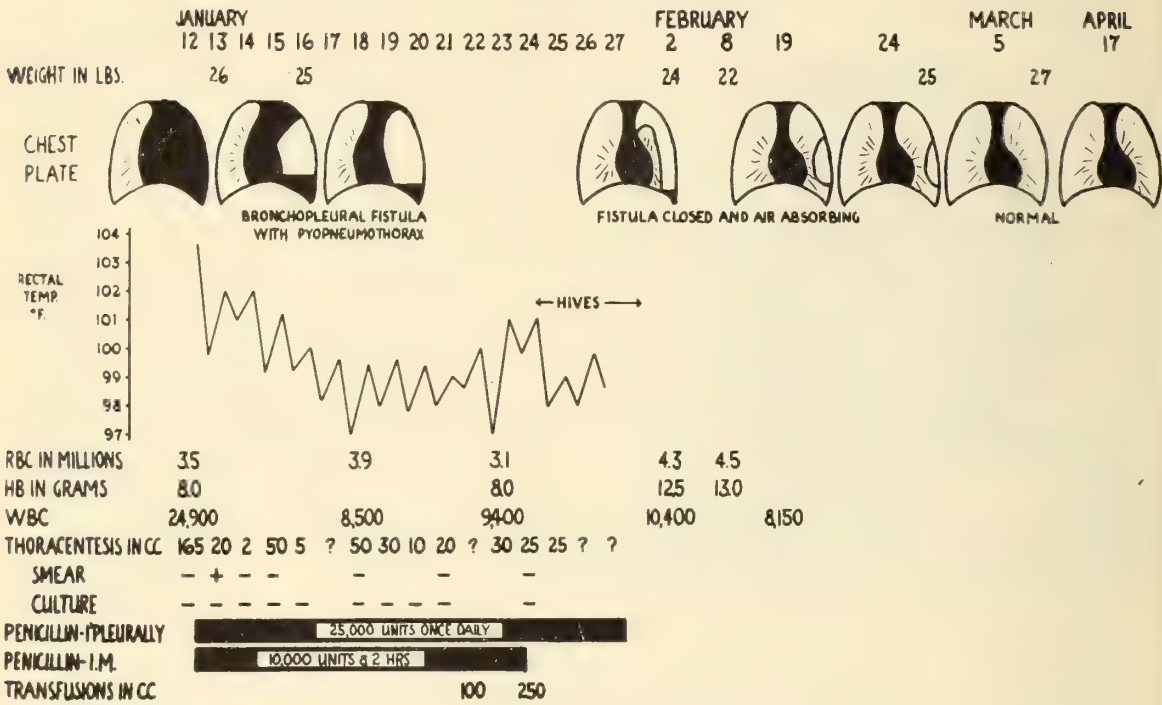


Fig. 9: Empyema thoracis treated without surgical drainage.

STAPH ALBUS EMPYEMA—SAID TO BE POST-PNEUMONIA  
HAD BEEN ASPIRATED SEVERAL TIMES PRIOR TO ENTRY  
CASE F.Y. #86078 AGE 18 MONTHS

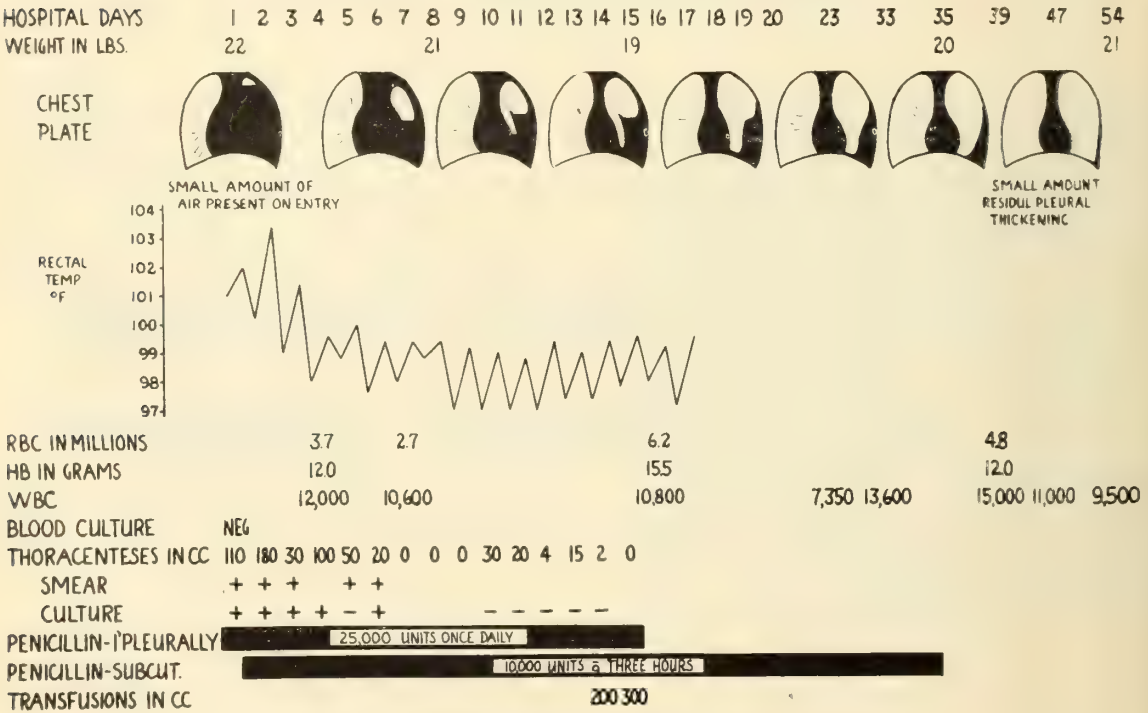


Fig. 10: Empyema thoracis treated without surgical drainage.



Figures 9 and 10 illustrate two cases of empyema treated by non-surgical means. Both cases were treated by simultaneous systemic and intrapleural penicillin. Each day a thoracentesis was performed, as much pus as possible aspirated, and penicillin (in a solution of 1000 units per c.c. of saline) instilled. Although everyone does not agree on the advisability of this mode of therapy, it has been quite successful in our experience. It goes without saying that it can be used only in those cases in which the pus is accessible to aspiration and thin enough to pass through a needle of large caliber.

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## SULFONAMIDES AND ANTIBIOTICS IN OTOLARYNGOLOGY

### THE GENERAL PRINCIPLES OF THEIR USE

GERALD F. JOSEPH, M. D.†

BATON ROUGE

There is probably no field in medicine which has been more profoundly affected by the introduction of sulfa drugs and antibiotics than otolaryngology. The otolaryngologist, whose time was once almost fully occupied with the treatment of acute infectious complications of upper respiratory diseases, now finds a great deal of his time spent on allergic disorders, rhinoplastic procedures, surgery of the neck, and peroral endoscopy. The changing nature of otolaryngologic practice was the theme of a recent address by Coates<sup>1</sup> before the American Academy of Ophthalmology and Otolaryngology. Even more significant is the fact that the American Board of Otolaryngology is now urging candidates for certifi-

cation to become proficient in endoscopy, allergic disorders and plastic surgery as well as the more conventional ear, nose and throat specialties.

## OTITIC DISEASE

Perhaps the most marked effect of changes in otolaryngologic practice as the result of new therapeutic methods is in the field of otology, in which the surgical treatment of acute mastoiditis and its complications has almost disappeared. Only occasionally today does the otologist see a patient with acute surgical mastoiditis in private practice, while in large public clinics hardly enough cases are seen for the young physicians to secure adequate training in surgery of the temporal bone. The situation is nationwide. It is especially noted in the South, however, where the milder climate has always kept the incidence of surgical mastoiditis comparatively low. On the very large otolaryngologic service at Charity Hospital of Louisiana at New Orleans mastoidectomy was once considered a surgical chore. Now the resident staff looks upon the operation as an unusual privilege.

The disappearance of surgical mastoiditis at this institution is statistically evident, and is out of proportion to changes in the hospital population. Over the 11 year period ending in 1946, a period during which sulfa drugs and antibiotics were introduced and popularized, the incidence has shown a steady decline (table 1). In 1936 there were 95 operations done for this condition. In 1946 only 13 were done. Furthermore, the rate of decline reflects almost directly the progress in development of these new therapeutic agents. Definite graphic plateaus indicate the introduction and use of each new group of drugs, though only after penicillin became available in adequate quantities did the drastic decline to the present low level occur.

Prior to the introduction and widespread use of penicillin there was a growing feeling that the sulfa drugs were beginning to fail. Streptococci are the principal causative micro-organisms in otitis media,<sup>2</sup> and sulfa-resistant strains were appearing. In-

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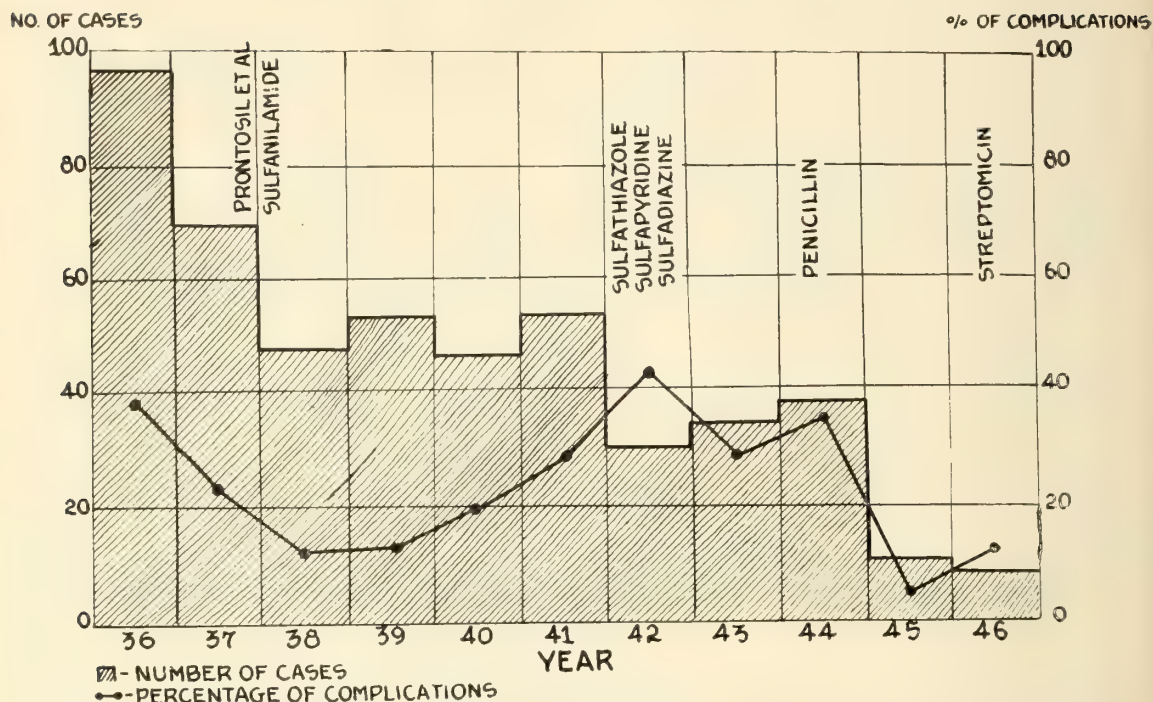


TABLE I: Showing the decrease in number of mastoidectomies done at Charity Hospital, New Orleans, during the eleven year period ending in 1946. Note the step-like decline in surgical mastoids with the introduction of each new group of drugs. Also note the tendency toward increase in percentage of complicated cases after each drug had been in use for a period of time.

stead of curing the otitic infection, in many cases the sulfa drugs were found to be masking symptoms.<sup>3, 4</sup> As a result, serious complications had often developed by the time it became evident that surgery was necessary.

An incident reported by von Christierson<sup>5</sup> in 1946 so well illustrates this point that it is worth repetition: During the winter of 1934-1944 a severe epidemic of streptococcal infections developed at a large Naval training station. A sulfa-prophylactic program was immediately begun and until mid-winter the results seemed excellent. At that time it was observed independently by several medical officers that sulfa-therapy did not seem useful in numerous cases, and it became clear that sulfa-prophylaxis had been responsible for this development of sulfa-resistant organisms. One immediate result was an explosive increase in the incidence of surgical mastoiditis, in many cases associated with grave complications, which developed without being detected be-

cause septic symptoms were masked by sulfonamide therapy. By January 1945 the proportion of surgical mastoiditis among well supervised patients with otitis media was 26.5 per cent, and a quarter of the patients who developed mastoiditis had dangerous intra-cranial complications. This alarming situation continued until April, at which time adequate supplies of penicillin became available for the treatment of patients who did not respond to sulfa therapy. The effect was immediate. In May, only 6.5 per cent of the patients with otitis media required mastoidectomy, while only one patient with mastoiditis had any complications.

This is not an isolated instance. Numerous episodes of the same kind have been reported by other observers.<sup>6, 7</sup> Quite evidently although the sulfa drugs and antibiotics are invaluable in the prevention and treatment of middle ear infections, they do not furnish complete protection, and constant supervision and observation of the



patient are necessary, especially when a sulfonamide is used.

Up to this time neither penicillin nor streptomycin have been used for sufficiently long periods to permit definitive conclusions, but warnings are already appearing that penicillin, like the sulfonamides, can mask symptoms in otitis media<sup>8, 9</sup>. The rapidity with which certain pathogens can develop a resistance to antibiotics has been demonstrated in vitro by Miller and Bohnhoff,<sup>10</sup> who were able to produce strains of streptomycin-resistant meningococci by only two or three transfers into agar containing increasing concentrations of the antibiotic. Resistance to penicillin, while less rapidly developed, was also apparent after remarkably few transfers. Both clinical and experimental observations, in short, almost make one fear that lack of material at this time for training otolaryngologists in temporal bone surgery may be felt at some future date unless new antibiotics are constantly developed to keep ahead of the development of resistant pathogenic microorganisms.

*Chronic Middle Ear Infections*: Chronic infections of the middle ear respond only equivocally to sulfa drugs and antibiotics. The best results have followed their local use. Kopetzky<sup>11</sup> reported some benefit from the use of a digesting mixture containing urea and sulfathiazole in a glycerine base, and there have been other isolated reports of good results from the introduction of penicillin-containing solutions into the middle ear under pressure or by means of Proetz displacement through the aural canal and Eustachian tube.<sup>12</sup> The best results, however, are not striking.

Collins and Hughes<sup>13</sup> probably have found the correct explanation of the poor results of these new drugs in chronic infections of the middle ear as their bacteriologic studies, show that the micro-organisms responsible for most cases of middle ear infection are not susceptible to either penicillin or the sulfonamides. Mixed infections are common, and for this reason it is important to make repeated bacterial checks

in cases in which this form of therapy is used. It is quite possible for a gram-positive strain to be controlled while the role of invader is taken over by a gram-negative pathogen not previously detected. In the absence of serial smears and cultures such cases are frequently set down as therapeutic failures.

Two instructive cases were recently observed on the Charity Hospital service of the Louisiana State University School of Medicine. Both patients presented chronic otorrhea with acute exacerbations. All types of treatment, including the administration of a sulfonamide and penicillin by local and systemic routes, had been ineffective. One patient, a 7 year old child, had required mastoidectomy twice in the preceding year for subperiosteal abscess. After the last operation the wound had failed to close and three attempts at secondary repair had been unsuccessful. When a culture report was obtained, it showed a small growth of gram-positive cocci with swarming *Bacillus proteus*. Streptomycin used as frequent irrigations had the ear dry within one week and the wound went on to uncomplicated closure.

The second patient, an adult negro woman, had an acute flare-up of an old chronic otitis media. Although she showed some response to penicillin, she continued to run a low grade fever and to show some local signs of mastoiditis. Mastoidectomy was under consideration, on the basis that penicillin might be masking the development of complications, when a culture was reported showing overwhelming *Bacillus proteus* growth with a small element of gram-positive streptococci. As in the first case, streptomycin, in this instance by the intramuscular route, produced prompt results. Evidence of mastoiditis subsided rapidly and operation was not required; there has been no evidence of recurrence over a long period of observation in the outpatient clinic. It is probable that in both of these cases gram-positive cocci were originally present in large numbers but that, after penicillin therapy, *Bacillus proteus* assumed

the major role and continued unchecked until controlled by streptomycin.

*Otitis Externa:* This condition, while it responds well in some instances to sulfonamides and antibiotics, whether used locally or systemically,<sup>8, 9, 14, 15</sup> is not one of the diseases in which either the treatment or the outcome has been radically altered by their introduction. This is not true when the infection spreads beyond the ear canal and a cellulitis of the scalp or face develops or when a lymphadenitis or lymphangitis appears as a complication. In such cases the new forms of therapy are extremely effective. In the uncomplicated cases of so called otomycosis however, they are not of great value, probably because a gram-negative organism is so often the pathogen in these infections. In such cases streptomycin should be of great help when available in sufficient quantities.

#### PHARYNGEAL AND RELATED INFECTIONS

In acute infections of the pharynx and related areas excellent results can be expected from the use of the sulfonamides and penicillin. The regional blood supply is good, and medications administered systemically can readily reach the site of disease. Even the local use of these drugs, through the medium of pastilles or lozenges, should be useful. These expectations seem borne out by a number of early reports on their use in tonsillitis, peritonsillitis, and pharyngitis.<sup>14, 15, 16, 19</sup> Later, more careful analyses, on the other hand, suggest that the results may be less spectacular than was originally supposed. Spink<sup>17</sup> and his associates feel that the sulfonamides are of questionable value except in severe infections of the pharynx with toxic manifestations, and indicate that the rate of relapse after both sulfa therapy and penicillin is exceedingly high. Clodfelter,<sup>18</sup> in a well controlled study, noted that patients who had been given a sulfa drug had more rapid relief from symptoms of tonsillitis or pharyngitis but suffered from secondary rises in temperature and were ill longer than patients who were not thus treated.

Vincent's ulcer of the tonsils is one infection in this area which responds almost

miraculously to small doses of penicillin.<sup>21</sup> Within a few hours after the intramuscular administration of as little as 25,000 Oxford units, the lesion has sometimes completely disappeared. To avoid relapse, however, it is recommended that treatment consist of two doses of 50,000 units each, at three hour intervals. Subsidence of symptoms occurs in most cases within four to six hours after treatment is begun, and practically always the lesion will completely disappear within a week without further care of any kind. This disease is a striking illustration of the value of the antibiotics when the causative lesion is highly susceptible to them.

Although promising results from the use of lozenges and pastilles containing sulfa drugs or penicillin are found in the literature,<sup>22</sup> doubt is expressed as to the actual value of this type of therapy, and it is not customary to rely upon these methods in the treatment of severe infections. Probably most patients, if not all, would fare just as well if lozenges and pastilles were omitted. It has been shown by McGregor and Long<sup>20</sup> that the salivary flow is such that a considerable amount of the contained drug may reach the tonsils from lozenges, but that the pharynx does not receive a sufficient salivary bath to be affected by a drug contained in a tablet held in the mouth. If the physician desires to use pastilles for pharyngeal disease, it is suggested that sufficient of the drug be contained in it to result in a detectable blood level from absorption in the alimentary tract.

#### LARYNGITIS

Penicillin and the sulfonamides are of value in acute infections of the larynx, just as in acute infections elsewhere, if the causative organisms are susceptible to these. This is particularly true of the types of acute laryngitis in children which results in croup and which may extend into the trachea in the form of laryngotracheobronchitis. When these patients require tracheotomy, instillation of a few cubic centimeters of salt solution containing penicillin into the tracheotomy tube every two or three hours serves to keep the bronchi



moist, controls local infections, and speeds recovery.

Aerosol penicillin<sup>23</sup> has been suggested as beneficial in acute laryngitis, but the drying effect of forced inspirations of air or oxygen may overbalance the benefit derived from the antibiotic. In tuberculosis of the larynx Figi's success<sup>24</sup> with intramuscular streptomycin has stimulated clinics all over the country to use the drug in this disease. It seems to give good results, but the rule still holds that the larynx will not remain healed unless the sputum becomes negative and the pulmonary lesion is arrested.

#### NASAL AND SINUS INFECTIONS

Penicillin and sulfa drugs have been used systemically and locally, with some success by both routes, in the treatment of infections of the nasal passages and the paranasal sinuses.<sup>8, 9, 14, 15</sup> It is reasonable to expect that they would benefit an acute hyperemic sinusitis if they were used systemically before the stage of suppuration. After empyema of the cavity develops, on the other hand, drainage by some means is necessary to effect a cure.<sup>25</sup> Definite improvement is likely to follow their use by lavage, by cannulization, or sinus puncture, or by the Proetz displacement method, but it is hard to evaluate their exact role. Simple drainage by lavage with saline solution will greatly benefit in most instances of sinus empyema, and the value of the addition of any bacteriostatic agent is questionable. Even in a diseased sinus the action of ciliated mucous membrane will quickly expel anything introduced into the cavity, while penicillin and the sulfonamides, to be effective, must remain in contact with the infectious organisms at least two or three hours. These drugs may be of some value if the sinus ostium is blocked, so that the drug used cannot escape, but the sinusitis, in that event, will not clear up until the occlusion is relieved. In other words, though the sulfonamides and antibiotics may be useful in sinus disease, certain factors limit their value and make their role in an ultimate favorable outcome at least doubtful.

The incorporation of antibiotics and sulfa

drugs into nose drops has achieved popularity in recent years, and at the present time many commercial preparations are available which combine these agents with a vasoconstrictor. The value of such preparations is questionable, for nose drops do not remain in contact with the inflamed nasal surfaces long enough for them to be effective.<sup>25, 26, 27</sup> Penicillin in weak solutions is known to be harmless to the nasal mucosa,<sup>26</sup> and its use, aside from possible unpleasant local sensitivity reactions, is not objectionable. The same cannot be said of the sulfonamides. A number of commercial preparations containing soluble sodium salts of sulfonamides are highly alkaline and they exert a caustic effect in the nose<sup>28</sup> which is destructive to the nasal mucosa and correspondingly harmful to the patient. Any nose drops with a pH over 6 are to be avoided.<sup>27, 29</sup>

In chronic sinusitis, which is often the result of an individual allergic response or of poor mechanical drainage to the infected sinus, antibacterial agents have proved of little value. A chronic infection may be helped during an acute exacerbation by the systemic administration of penicillin or sulfa drugs, but it cannot be said that their use improves the patient's chances for ultimate cure of the chronic state, in which carefully planned surgery and desensitization therapy are the most likely roads to relief.<sup>27</sup> In this condition, just as in chronic otorrhea, the explanation is undoubtedly the presence of nonsusceptible pathogens.

Although promising results have been reported from the use of areosol penicillin in the treatment of sinus infections,<sup>23</sup> this is another condition in which it is questionable whether the means of administration has much to do with the benefits observed. The blood level achieved by absorption of the drug in the pulmonary alveoli must be credited with any good results. It was shown long ago<sup>29</sup> that air passing through the nose does not enter the sinuses, while the volume of air exchanged between the sinuses and the nasal passages is minute. Proetz has estimated that it requires many hours for a single complete change in the

air content of a sinus to occur as the result of the respiratory motion of nasal air. Studies are now being conducted at the Columbia University College of Physicians and Surgeons in the treatment of sinus disease with aerosol penicillin by means of an alternating positive and negative pressure apparatus. There are obvious dangers inherent in such a method, but it offers a rational approach to the problem, and it may prove very valuable.

#### BRONCHOPULMONARY INFECTIONS

The otolaryngologist whose practice includes bronchoesophagology has found penicillin and the sulfa drugs useful in this field.<sup>30</sup> The intrabronchial instillation of penicillin solutions (as well as of streptomycin) through the bronchoscope in the treatment of chronic bronchopulmonary infections such as lung abscess and bronchiectasis has met with great success. Sulfa drugs, in the form of powders, have been insufflated into the respiratory passages by the same route, but caking of the powder has been reported and the method is obviously undesirable. Antibiotic aerosols find their greatest usefulness in this type of infection. They have been utilized for both palliation and cure, as well as in preparation for thoracic surgery, and the results have been almost uniformly favorable.

#### PENICILLIN BY THE ORAL ROUTE

In the opinion of many observers penicillin by the oral route should be more useful in otolaryngology than in many other fields of medicine. A large proportion of patients with otolaryngologic disorders are not seriously ill and can remain ambulatory. For these reasons, in spite of the variable results to be expected, oral administration of penicillin seems justified. Some reports are distinctly encouraging, and Lierle's<sup>31</sup> experimental studies have put the method on a logical basis. The blood levels produced by oral administration are usually adequate to control simple infections and prevent complications, and if the patient is kept under close observation, there can be no objection to the method on the ground of safety. The use of Romansky's beeswax and oil formula<sup>32</sup> is more logical, but many

patients object to injections by needle for conditions which are not disabling.

#### DISCUSSION

It probably seems somewhat confusing for a communication which began with the statement that the sulfa drugs and antibiotics have materially altered the practice of otolaryngology to be chiefly concerned with a discussion of the limited effectiveness of these agents in the common infections of the ear, nose and throat. Some comment is obviously needed to clarify the situation.

It should be noted first of all that most of this presentation has had to do with the use of chemotherapy and antibiotic therapy in such simple infections as tonsillitis, sinusitis, laryngitis and pharyngitis, all of which may be termed "office practice" diseases. In these conditions the value of the new methods is still under debate. The literature is confusing, and my purpose in this communication has merely been to analyze it and edit it, so to speak, for the benefit of those who are not otolaryngologists.

In the prevention and treatment of the serious complications which may result from such minor infections as those mentioned, there is no doubt of the value of these new agents. They are extremely useful. The control of mastoiditis from otitis media is an outstanding example of their value. Extension to the mastoid air cells and adjoining regions still occurs in spite of their use, when the causative microorganisms are drug-resistant, but on the whole, mastoiditis is now a waning disease, intra-cranial complications are relatively infrequent, and their lethality has been greatly reduced. Meningitis, cerebral abscess, lateral sinus thrombosis and petrositis can usually be cured by the use of the antibiotics or sulfonamides, combined, if necessary, with appropriate drainage. Osteomyelitis of the frontal bone, and cavernous sinus thrombosis, which formerly were dreaded complications because of the high mortality associated with them, now usually can be prevented or, if they occur, can often be cured by the use of these new remedies. Hill,<sup>33</sup> in his recent appraisal



of Mosher's "seven great problems in otolaryngology", listed them as among the problems which are approaching solution. What is true of mastoiditis is also true of all soft tissue and intracranial complications of infections of the ear, nose and throat. They are usually preventable by the early use of the sulfa drugs and antibiotics and if they develop, they can usually be cured, often without surgical drainage, by use of the same agent. It is therefore fair to say that otolaryngology is a different specialty today from what it was 10 years ago.

## SUMMARY

1. The advantages and limitations of the sulfonamides and antibiotics have been discussed in relation to various otolaryngologic conditions.

2. The limited usefulness of these agents in the so-called "office practice" diseases has been pointed out, and their extreme value in serious complications which may result from these minor infections has been emphasized.

3. The risk that sulfonamides and antibiotics may permit serious complications to develop by masking symptoms in mastoiditis must be borne in mind by every physician who uses them.

4. In spite of the fact that these new agents are not "cure-alls" they have completely altered the character of otolaryngologic practice, and when properly employed, they have an enormous prophylactic and therapeutic field of usefulness.

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## ADULT HYPOTHYROIDISM AND MYXEDEMA

### A REVIEW OF THE DIAGNOSTIC DATA IN 151 CASES

NORMAN BURNSTEIN, M. D.†

NEW ORLEANS

In this study the inclusive term adult hypothyroidism is applied to all cases of hypometabolism believed to be due to a decrease of thyroid hormone; hypothyroidism of severe degree characterized by marked reduction of the basal metabolic rate and the classic clinical features of severe hypothyroidism are here classified as myxedema.

#### TOTAL INCIDENCE

In the 11 year period from 1935 through 1945, a total of 151 cases of adult hypothyroidism and myxedema were admitted to the Charity Hospital. During this period the total number of admissions to the hospital, exclusive of newborns, was 553,240; the incidence of hypothyroidism was thus 0.0002 per cent. Of the 151 patients, 43, or 22 per cent, had frank myxedema. Reports from institutions in other parts of the United States give a higher incidence than the figures noted here. Means<sup>1</sup> noted that at the Massachusetts General Hospital patients with myxedema constituted 0.08 per cent of the total number admitted to the wards. Shepardson and Wever<sup>2</sup> found an incidence of 0.04 per cent of admissions in the University of California Hospital in 1934, and at the Mayo Clinic<sup>1</sup> in 1935 patients with myxedema constituted 0.07 per cent of total hospitalized patients.

#### RACE

Of the 151 cases, 111 occurred in white persons and 40 in negroes, during a period when 283,516 whites and 269,724 negroes were admitted to the hospital. Hypothyroidism was thus about three times as common in persons of the white race. Of the cases of myxedema, 35 were in whites and eight in negroes. A survey of the literature did not reveal data regarding the compara-

tive incidence of hypothyroidism in the white and negro races.

#### SEX

One hundred and thirty-one of the 151 patients, or 86 per cent, were females. Thirty-one of the 43 cases of myxedema, or 72 per cent, occurred in females. Means<sup>1</sup> in studies at the Massachusetts General Hospital found an incidence of 82 per cent in females in cases of myxedema. Kohlhas<sup>3</sup> found a ratio of 10 males to 40 females, and Thompson<sup>4</sup> found similar results in his report.

#### AGE

The age incidence is listed in table 1, which shows that half of the cases occurred in individuals below the age of 40, and 40 per cent below the age of 30. Kohlhas<sup>3</sup> found the average age in 50 cases studied to be 34 years. Thompson<sup>4</sup> states that the disease occurs more frequently in the fourth, fifth, and sixth decades of life.

TABLE 1  
AGE INCIDENCE

Age	Number of Cases:	
	Hypothyroid	Myxedema
18 - 30 .....	46	15
30 - 40 .....	31	6
40 - 50 .....	17	6
50 - 60 .....	10	8
Above 60 .....	4	8

#### PRESENTING SYMPTOMS

In table 2 the complaints of these patients and their frequency of occurrence are listed. The onset of the symptoms was slow in all cases; in 10 cases symptoms were first noted during or shortly after pregnancy. The presenting complaints were most frequently referable to the genital, gastrointestinal, neuromuscular, and cardiovascular systems. Symptoms of greatest frequency in myxedema were headaches, constipation, fatigue, backache, abdominal pains, and general body aches and pains. Lerman<sup>5</sup> in 1933, in a review of 77 cases of myxedema, noted similar findings in the symptomatology of myxedema. The above findings are in agreement with the findings of Rose,<sup>6</sup> Reilly,<sup>7</sup> and Pullen<sup>8</sup> that the presenting symptoms in cases of mild and moderate hypothyroidism may be manifold and nonspecific.

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TABLE 2  
SYMPTOMATOLOGY

Symptoms	Hypothyroidism		Myxedema	
	Cases	Per cent	Cases	Per cent
Number			Number	
Irregular menses	33	32	3	7
Abdominal pains	31	28	11	26
Headaches	26	24	15	35
Anorexia	23	21	5	12
Nausea	21	20	9	21
Increased menses	18	17	2	5
Fatigue	17	16	19	44
Weight loss	15	15	7	16
Constipation	16	15	17	40
Backache	16	15	13	30
Nervousness	14	13	4	9
Weight gain	15	14	7	16
Vomiting	15	14	5	12
Cardiac pains	14	13	10	23
Lethargy	13	12	6	14
Qualitative dyspepsia	11	10	4	9
Cardiac palpitations	10	10	5	12
Epigastric fullness	9	8	6	14
General aches and pains	9	8	10	23
Dizziness	8	7	7	16
General malaise	8	7	5	12
Amenorrhea	8	7	2	5
Memory impairment	7	6	7	16
Decreased menses	7	6	0	0
Sensitivity to cold	6	4	7	16
Increased lacrimation	6	4	3	7
Dyspnea	5	4	1	3
Sleepiness	4	3	3	7
Diarrhea	2	2	7	16
Earache	3	2	0	0

## PHYSICAL SIGNS

The physical signs believed to be associated with the hypothyroid state are listed in table 3. The findings stress the fact that physical findings of a characteristic nature are much more frequently found in the cases of myxedema than in varying lesser degrees of hypothyroidism.

## OTHER DISEASES

In the cases of hypothyroidism without frank myxedema, 53 per cent of the patients had other diseases which contributed importantly to the clinical picture, the most frequent being gynecologic disorders and gallbladder disease. On the other hand, only 18 per cent of the patients with frank myxedema had other significant disorders. Table 4 lists in order of frequency the primary diagnosis recorded.

## LABORATORY DATA

The basal metabolic rates prior to the institution of replacement therapy are listed

TABLE 3  
PHYSICAL SIGNS

Physical Signs	Per cent of Cases:	
	Hypothyroid	Myxedema
Obesity	37	14
Enlarged thyroid gland	24	5
Hypotension	15	14
Cardiac enlargement	10	11
Coarse dry hair	10	5
Myxedematous facies	8	22
Edema of eyelids	8	21
Dry skin	8	37
Edema of face	7	37
Thick skin	4	16
Edema of hands	3	19
Thick tongue	3	14
Loss of body hair	3	16
Thin eyebrows	3	10
Coarse rough skin	2	10
Brittle nails	1	0
Cool skin	1	2
Pallid skin	0	9

TABLE 4

## DIAGNOSES

Primary Diagnosis	Number of Cases:	
	Hypothyroidism	Myxedema
Hypothyroidism or myxedema	58	35
Gynecologic disorders	20	1
Nephritis	3	2
Cholecystitis	7	0
Goiter, non-toxic	6	1
Postoperative thyroidectomy	6	2
Tuberculosis	2	0
Diabetes mellitus	1	1
Hookworm disease	0	1

in table 5. Seventy-seven per cent of the patients with frank myxedema showed B.M.R. readings more than 20 per cent below normal.

TABLE 5  
DISTRIBUTION OF BASAL METABOLIC RATES

Basal Metabolic Rate	Per cent of Cases:	
	Hypothyroidism	Myxedema
—5 to —10	17	0
—10 to —20	29	7
—20 to —30	14	23
—30 and below	0.9	54
Not recorded	39	16

Blood cholesterol values were capricious in this series, probably because the method used for this determination was not reliable. In almost half of the 21 cases of myxedema in which blood cholesterol was determined, the level was below 200 mg./100 c.c.

The results of blood counts are shown in

table 6. In 42 per cent of the cases of frank myxedema, significant anemia was present. Six cases of myxedema showed a hyperchromic macrocytic type of anemia.

Electrocardiographic abnormalities compatible with or suggestive of hypothyroidism (low complexes, isoelectric T waves, prolonged QT interval) were noted in four cases of hypothyroidism and 14 cases of myxedema.

TABLE 6

	Per cent of Cases:	
	Hypothyroidism	Myxedema
Total red blood cell count		
Above 3.5 million .....	23	23
Below 3.5 million .....	9	42
Hemoglobin		
Above 10.5 gm. ....	9	42
Below 10.5 gm. ....	23	20

## SUMMARY

1. A study of 151 hospitalized cases of hypothyroidism and myxedema occurring in an 11 year period at a large Southern hospital are reviewed.

2. The relatively low incidence of these disease states in this region of the country is noted in contrast to much higher figures elsewhere.

3. The higher incidence of occurrence in the white race than in the negro race is emphasized.

4. The cases studied here occurred at an earlier age than in some other series.

5. Females had the disease more often than males, in general agreement with the finding of others.

6. Typical signs, symptoms, and laboratory data lend further emphasis to the general findings recorded in the literature.

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## HUMAN ISOIMMUNIZATION

J. W. DAVENPORT, JR., M. D.†

NEW ORLEANS

Some of the clinical phenomena of heteroimmunization were observed as early as 1667 following the repeated transfusion of sheep blood into human recipients. The French surgeon, Denys, wrote of a patient, who, following a second such transfusion, exhibited a rapid pulse, nausea, profuse sweating and pain in the kidney region, followed the next day by passage of urine described as "black".<sup>1</sup> These are recognized as signs and symptoms resulting from the transfusion of incompatible blood and it is known that antibodies in the patient's blood initiate the unfavorable response by hemolyzing the transfused red cells, the black urine arising from the presence of hemoglobin pigments derived from the laked erythrocytes.

Here was an example of the sensitization of one species by an antigen present in a different one. This is relatively easy to demonstrate in laboratory animals and is the basis of preparing typing fluids for the identification of the M and N factors in human blood.

Isoimmunization, or sensitization within a species, was first described by Ehrlich and Morgenroth in 1900. By cross-transfusions between goats, they were able to demonstrate the development of immune antibodies in the recipients. The antibodies served to differentiate the bloods of individuals belonging to the same species. Applying the same methods, as *in vitro* procedures, Landsteiner<sup>2</sup> demonstrated in humans the existence of the normal isohemagglutinins anti-A and anti-B and established the identity of the four major blood groups, A, B, AB and O. This discovery stands as a genuine epoch in science because it not only made possible safe blood transfusion therapy, but also serves as the basis of all our

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accumulated knowledge of human isoimmunization.

Sensitization to the Rh factor of Landsteiner and Wiener is the best known example of isoimmunization in man and is recognized as the etiologic agent in some 92 per cent of all cases of hemolytic disease of the newborn and of intra-group hemolytic transfusion reactions.<sup>3</sup> Investigations in this field have also served to redirect attention to the presence of several different agglutinogens in human erythrocytes. Nearly all of the factors identified to date have been known to behave as antigens, albeit rarely in the case of some of them. The rare, and at times obscure, sensitizations deserve some consideration because they are concerned in the 8 per cent of cases of hemolytic disease and transfusion reactions not due to Rh.

The major group specific substances, A and B, are not confined to the erythrocytes but are present in almost every internal organ, especially glandular tissue. A large majority of individuals, apparently as an hereditary trait, also secrete their group specific substance in saliva, gastric juice and amniotic and other body fluids. Characteristic of the A-B groups is the presence of the normal isohemagglutinins, anti-A and anti-B, in plasma or serum. These are globulins and can be demonstrated in high protein body fluids such as milk, lymph and transudates.

The higher incidence of abortions and miscarriages in group incompatible matings was noted two decades ago and re-emphasized in recent years.<sup>3, 4</sup> In view of the many instances in which mother and fetus are group incompatible one would expect a considerable incidence of hemolytic disease due to differences in major group. That such is not the case is due to the fact that a majority of unborn infants secrete their group specific substance and the presence of this in amniotic fluid and fetal circulation serves as a protective mechanism by neutralizing or absorbing the antagonistic maternal isohemagglutinins. Thus, in the 8 per cent of erythroblastosis in offspring of Rh+ mothers, not more than 2 per cent probably

are due to A or B hyperimmunization. These cases, when seen, however, are clinically indistinguishable from those caused by typical Rh sensitization of Rh— mothers.

Recently I reported such a case in which the affected infant and mother were both Rh+ , the baby belonging to group B and the mother to Group O, with the significant findings of a marked specific increase in maternal anti-B agglutinin and a negative test for B substance in the neonatal serum.<sup>5</sup> Unlike A and B, these agglutinogens are confined almost entirely to the erythrocytes and natural isohemagglutinins are very rarely encountered, while transfusion isoimmunization to M or N is but slightly more frequent.<sup>9</sup> These factors are identified by means of heteroimmune sera prepared from animals immunized to human M+ and N+ bloods.

M and N, like A and B, are inherited as simple Mendelian dominants, but unlike A and B, are never both absent. There are, then, three types of MN bloods in humans: M,N, MN. While subvarieties of the A factor are well known, such is not the case for M and N, although a subtype of N has been described.

The relationship of M and N is important in itself and further serves as a useful analogy in appreciating the reciprocal kinship between the Rh and Hr factors.

In 1928 Landsteiner and Levine<sup>6</sup> made an important contribution when they discovered yet another agglutinable factor in human erythrocytes. This agglutinin, named P, apparently is confined to the erythrocytes and natural human anti-P agglutinins are extremely rare, although the sera of horses and pigs often exhibit agglutinins specific for the factor. It is inherited as a simple Mendelian dominant and the existence of subtypes has been suggested. On infrequent occasions the P factor behaves in an antigenic manner and a recent case of P isoimmunization was reported by Wiener and Unger in 1944.<sup>8</sup>

The complex or mosaic nature of the Rh factor is presently well verified. Essentially it consists of three subfactors designated Rh<sub>0</sub> Rh' and Rh".<sup>10</sup> Each of these is capable

of antigenic behavior following entrance into the circulation of an individual lacking it. The identity of the subfactors was established by the discoveries of human isoimmune anti-Rh sera giving respectively 85, 70 and 30 per cent positive reactions against erythrocytes of white individuals in general. Just as the three Rh agglutinogens co-exist in various combinations, determining the eight major subtypes, so the three Rh antibodies may be and are found singly or variously together in the serum of an isoimmunized person.

As Levine has repeatedly and so clearly shown, the anti-Rh<sub>0</sub> (85 per cent) serum is clinically of greatest value. The existence of the Rh subtypes explains some of the rare cases of erythroblastosis in infants of Rh+ mothers. In these instances the father and affected baby possess a subfactor absent from the blood of the mother, although she may possess both of the others. Intermediate Rh subfactors have been encountered, but to date constitute a rarity.

Originally it was believed that Rh was confined to the erythrocytes and was not secreted. However, the presence of Rh agglutinogens in certain organs and in saliva, gastric juice and amniotic fluids of Rh+ individuals has been demonstrated in a small number of cases.<sup>11, 12</sup> Secretion of Rh substance serves as one explanation of the occasionally normal Rh+ infant born to an isoimmunized Rh— mother. Further, this information brings within the realms of probability the development of a non-antigenic means of neutralizing Rh antibodies *in vivo*, a procedure which should cause a marked decrease in neonatal morbidity and mortality due to hemolytic disease of the newborn.

In 1941 Levine began the long series of studies which lead to our present extensive knowledge of the Hr factor.<sup>3</sup> In the early stages of this investigation, involving erythroblastosis in infants of Rh+ mothers, he established the existence of an agglutino-gen bearing a reciprocal relationship to Rh and to it gave the apt name, Hr. More recent work by Levine and others has established the complex nature of Hr and the

presence of three Hr agglutinogens Hr<sub>0</sub>, Hr' and Hr'', each corresponding to a respective Rh factor. In other words, a blood which is Rh— is Hr+. Further, the red cells of some people contain both Rh and Hr agglutinogens and some contain only Hr, the latter being the so-called "true" or "complete" Rh negatives. Levine was first to point out the analogy of Rh and Hr to M and N. Thus three MN types are possible: M,N, MN, types M and N being homozygous. Similarly three Rh-Hr types are possible, Rr, Hr and RhHr. Some bloods are homozygous for Rh (RhRh), some likewise for Hr (HrHr) while many individuals possess both factors and are therefore heterozygous (RhHr).

Hr is as highly antigenic as Rh, but few cases of Hr isoimmunization are seen due to the high incidence of heterozygous (RhHr) people. In a case of erythroblastosis still being studied, we found the father, two older children and the affected infant were all Rh+ Hr+ (thus heterozygous) while the mother was found to be Rh+ Hr— (thus homozygous for Rh) and to exhibit anti-Hr antibodies in her serum. Levine's general rule applied in this case, to wit: "the fetus must be heterozygous for the factor to which the mother is isoimmunized."

Actually we have only touched upon the subject of human agglutinogens and isoimmunization. A number of other factors have been identified in human blood but thus far seem of no clinical significance. It must be remembered that not all of these substances and their sub-forms are present in the erythrocytes of any one individual so that the possible permutations and combinations are almost infinite and from the original four major groups of Landsteiner we have progressed to identification of several hundred types of human blood.

#### CONCLUSION

This general statement may be made regarding human isoimmunization: Certain agglutinogens present in human erythrocytes at times behave as antigens, some to a greater degree than others; transfer of antigen takes place by blood transfusion



and/or pregnancy, the erythrocytes of the donor (fetus) possessing one or more agglutinogens absent from the erythrocytes of the recipient (mother).

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## NEW METHOD OF TREATING PEPTIC ULCERS WITH PENICILLIN GASTRIC DRIP

### PRELIMINARY REPORT\*

RICHARD W. YOUNG, M. D.

BATON ROUGE

The purpose of this paper is to bring before the staff members of this hospital the striking results obtained in treating four cases of proved peptic ulcers by a continuous gastric drip of penicillin in soda water for ten days.

I fully realize that the reporting of four cases is of little or no statistical value; however, the results were so striking that I feel justified in making this report.

As far as I can ascertain, this method of treating peptic ulcers with penicillin gastric drip has never been reported, and inasmuch

as it is simple and of no danger to the patient it is worthy of extensive use in this type of disease.

The treatment is based on the theory that gastric ulcers are infected and the irritating factors of the stomach, namely, food and acid, interfere with the opportunity to heal. Therefore, the reasoning behind this method is simple. Remove the irritating factors and apply directly to the ulcer some non-irritating and non-toxic antibacterial agent. This we have in penicillin dissolved in soda water.

The method I have used on these cases was definitely to establish the exact location of the ulcer by fluoroscopy and x-ray. A small soft stomach tube was passed into the stomach via the nose and fixed in position so the stomach end is above the ulcer. The outside end is attached to a 1000 c.c. drip bottle suspended from an infusion stand and containing 200,000 units of penicillin dissolved in 1000 c.c. of tap water to which have been added two teaspoonfuls of bicarbonate of soda. This is regulated to drip continuously at the rate of 60 drops a minute. In all cases it was continued night and day for eight to ten days. The patient is not allowed to take anything by mouth except small sips of water to keep the throat moist, this only when absolutely necessary. Infusions of 5 per cent glucose in 1000 c.c. of normal saline are given once each day. Codeine and luminal by hypodermic were used occasionally at night to insure adequate rest. Nothing else was given the patient.

The criteria used to know when to remove the tube were daily gastric analysis, symptomatic relief, and, finally, fluoroscopy and x-ray demonstrating absence of the ulcer.

#### CASE NO. 1

Mr. M. C., aged 42, was admitted to the hospital on June 3, 1946, with a history of pain in the epigastrium accompanied by nausea and vomiting. Patient stated that he had been under treatment for stomach ulcer for over a year. X-ray diagnosis was made and he had been on a diet ever since with very little relief. Two days before admission he began to suffer severely from pain and nausea which had become unbearable. Vomiting was clear, very acid, no blood.

*Physical examination* revealed a well nourished

\*Read before the staff of the Baton Rouge General Hospital July 16, 1947.

white male whose weight was 150 pounds, not acutely ill. The head was negative; chest negative; lungs clear; heart normal. B. P. 140/90. Abdomen was soft. There was a marked tenderness over epigastric region extending down to the umbilical region; genitalia and extremities normal.

*X-ray and fluoroscopic examination:* On the posterior wall of the pyloric canal is a residual fleck which is persistently observed when the barium is partially expressed. There is localized tenderness over the area. The fleck is believed to represent the crater of an active gastric ulcer.

*Laboratory:* Gastric analysis: Total acidity 70; HCl free 60. Blood: Kahn and Wassermann negative. Red blood cells 4,050,000; white blood cells 5950; hemoglobin 75 per cent; S. L. 41; L. M. 5; P. N. 53; E. 1; negative malaria; urine negative; temperature normal.

*Treatment:* Using soft stomach tube, via nose, the penicillin gastric drip was started June 10, 1946, with 1000 c.c. tap water, two teaspoonfuls of bicarbonate of soda with 200,000 units of penicillin. A continuous drip, 60 drops per minute, continued for eight days. An infusion of 1000 c.c. of 5 per cent dextrose was given once daily.

*Progress:* Daily gastric analysis showed absence of free HCl with a total acidity averaging 15 per cent. There was relief of symptoms on the third day; no complaints; no hunger or thirst experienced by patient. The bowels moved daily without aid. On the morning of the ninth day the tube was removed and an x-ray made.

*X-ray and fluoroscopic examination, June 18, 1946:* No evidence of fleck. Slight angulation at pyloric-duodenal junction is attributed to scarring results from the healed ulcer. Patient was placed on a full diet with no return of symptoms.

*Follow-up:* Twelve months after discharge the patient had gained 40 pounds, had no symptoms, and stated he could eat anything he wishes without and symptoms or discomfort.

#### CASE NO. 2

Mr. M. C., aged 23, was admitted to the hospital on May 27, 1947 with a chief complaint of pain in the stomach, gnawing in character, relieved for a short time by drinking milk. He was unable to eat any solid food because of nausea. Had x-ray diagnosis of duodenal ulcer prior to admission. Examination revealed a white male not acutely ill, underweight, and extremely nervous. Head normal; chest normal; abdomen, marked tenderness in region of epigastrium; extremities and genitalia normal.

*X-ray report on June 7, 1947:* Findings reveal large fleck in first portion of the duodenum which did not disappear on pressure, and tenderness was elicited on palpation. Diagnosis: duodenal ulcer, moderate size.

*Laboratory:* Gastric analysis: Not reported from laboratory prior to treatment. Red blood cells 5,650,000; white blood cells 9,000; hemoglobin 90

per cent; S. L. 19; P. N. 80; E 1; negative malaria.

*Treatment:* Continuous penicillin gastric drip as described above was carried out for 10 days; one infusion daily of 5 per cent glucose, 1000 c.c. given.

*Progress:* On third day, complete relief of all symptoms was reported by the patient. Gastric analysis was reported free from HCl, total acidity of 5 on the third, sixth and eighth days. During treatment the bowels moved normally, no hunger or thirst experienced. Tube was removed on the morning of the eleventh day and x-ray and fluoroscopy made immediately after. Report: The findings revealed complete healing of the moderate size ulcer crater previously described with a slight cicatrization as a residuum.

The patient was placed on a full diet and, having no discomfort or symptoms, released from the hospital. A check-up on the case at time of reading of this paper. He states that he is eating anything he wants and has no discomfort, and he is working full time without fatigue.

#### CASE NO. 3

Mrs. D. T., aged 59, a white female gave a history of pain in the stomach for past 12 months, accompanied by nausea and occasional vomiting. She has had almost constant pain in stomach for past three months and she has been unable to eat anything except milk and cream; she has been very irritable and nervous. Patient stated that she was diagnosed duodenal ulcer by x-ray and admitted to a New Orleans hospital for six weeks, at which time she was given milk and cream and amphojel. She was relieved and came home three months ago. Since being home, a return of the symptoms occurred with a gradual increase in the severity. The day prior to admission she vomited a small amount of blood.

*Physical examination:* Well nourished white female, not acutely ill. Head normal; chest normal; lungs clear; heart normal; B. P. 148/84, pulse 80; temperature normal. Abdomen: no scars, marked tenderness of the epigastrium on slight pressure, no masses felt, liver and spleen not palpable; extremities normal.

*X-ray and fluoroscopy:* The duodenal cap exhibits a marked filling defect, indicating an ulcer of the first portion of duodenum. Six hours after the barium meal there is a retention of barium in the ulcer crater.

*Laboratory:* Gastric analysis: Total acidity 80, free HCl 60; urine, negative except for faint trace of albumin. Blood: white cells 7,150; S. L. 37; L. M. 3; P. N. 60; no plasmodia found.

*Treatment:* Penicillin gastric drip continuous for 10 days as previously described.

*Progress:* Complete relief of symptoms occurred on the third day. Patient tolerated the treatment well; bowels moved well throughout treatment, and after the fourth day she walked out on the sun porch daily, carrying her drip bottle which



she would hang up on an infusion stand and she would sit in a chair for two hours. She did not require any sedation at night to rest. Her daily gastric analysis revealed no free HCl and average total acidity of 15 units each day throughout the 10 days. Tube was removed on the eleventh day and x-ray and fluoroscopic report was as follows: There is evidence of a healed ulcer of the duodenum. On emptying, no fleck remains. This patient was placed on a full diet and thus far no discomfort or symptoms have occurred.

## CASE NO. 4

Mr. P. E. E., a white male, aged 51, was admitted to the hospital June 14, 1947, with a chief complaint of pain in the stomach of a burning character; nausea and eructation of very acid fluid, inability to eat anything without considerable pain and nausea. The symptoms began three months ago. Prior to that time he suffered quite a bit with indigestion. Has become very nervous and irritable. Past history is negative.

*Physical examination* revealed a white male, well nourished, not acutely ill, approximate weight 170. Head normal; chest normal; lungs clear; heart normal. B. P. 130/80. Abdomen: marked tenderness in epigastrium on palpation, no rigidity, no masses, liver and spleen not palpable. Genitalia and extremities normal.

*X-ray and fluoroscopic examination:* A moderately large fleck in the first portion of duodenum, persistent on compression, and marked tenderness on pressure. Diagnosis: active duodenal ulcer.

*Laboratory:* Gastric analysis: Total acidity 70, free HCl 55. Blood: red blood cells 5,700,000; hemoglobin 90 per cent; white blood cells 8,000; S. L. 26; L. L. 4; P. N. 69; E 1; negative malaria. Urine negative. Blood Wassermann negative.

*Treatment:* Penicillin gastric drip continuously for ten days as described above.

*Progress:* Complete relief of symptoms occurred on the fourth day. Daily gastric analyses showed a gradual decline the first three days to total acidity of 4, no free HCl. This remained low for an average of 4 to 6 total acidity, no free HCl. The treatment was tolerated well and bowels moved regularly after the second day. The tube was removed on the morning of the eleventh day. Immediate x-ray and fluoroscopic examination was made.

*Report:* No fleck visible. No tenderness noted by patient. Examination of the patient in both the erect and dorsal decubitus, with and without compression, fails to reveal the ulcer which was observed June 11, 1947. The findings suggest complete healing of the previously described large duodenal ulcer. The patient was placed on a full diet with no complaints or discomfort.

Follow-up at the time of reading of this paper: Patient stated he could eat anything and had no symptoms, that he was the happiest man in town. No tenderness could be elicited on examination of abdomen.

## CONCLUSION

I would like to emphasize again that this short series of cases in this preliminary report are not conclusive evidence by any means that this form of therapy is the last word, but the striking results warrant further investigation along these lines.

I hope that each member of the staff here tonight will feel free to discuss and criticize this therapy as he sees fit.

In conclusions I would like to thank Dr. Arthur Alexander and Dr. Lester Williams, radiologists, for their splendid help and cooperation with these cases, and Dr. Brinsfield King and Dr. Jack Bevens, pathologists, for their diligent cooperation.

## DISCUSSION

Dr. C. H. Mosely: Do you feel that patients get well quicker with this treatment than with amphotril or milk?

Answer: It is my impression that an ulcer is infected although there are different schools of thought on this. All I can say until more time goes by is that the patient gets well quicker with this treatment. I believe a patient could stand the treatment over ten days. However, this has been sufficient to complete healing in these four cases.

Dr. G. H. Riche, Jr.: Did you give the patients any sedation?

Answer: To the first patient, I gave codeine for first three days, but after that he did not need any. The third patient was given luminal twice the first two days after which she slept all night without any sedation.

Dr. J. D. Martin: Do you think that simply putting the patient to bed where he could get the proper rest and diet and could be removed from his environment would cure the patient as well?

Answer: Perhaps, but the time limit would be longer, while this treatment is short. The lady who stayed in a hospital six weeks on an amphotril and milk diet was cured in ten days with this treatment.

Dr. J. E. Toups: I would like to request that in the next case treated the penicillin be left out.

Answer: In the third case, as soon as acid disappeared on third day, I stopped the soda and gave pure penicillin and tap water. In the fourth case, soda was cut to 1 dram instead of 2.

Dr. R. B. Wallace: Do you think there is secondary infection around an ulcer?

Answer: That is the theory on which this treatment is based. Heretofore, the stumbling block has been acid in the stomach, which is the reason for using soda in order to neutralize the acid to the point where penicillin will be effective. It is well known that the antibacterial effect of penicillin

is destroyed by HCl in stomach, thus the soda bicarb. is used.

Dr. G. H. Riche, Sr.; Has the first patient been followed up?

Answer: Yes, for one year, with no symptoms or discomfort. The other patients have also been followed up, for a shorter period, of course. None has had a return of symptoms.

Dr. L. H. Stander: Because of the high incidence of malignancy, I should like to advise caution in the treatment of gastric ulcers in the stomach proper as it is a well known fact that gastric carcinoma does ulcerate. Early surgery for gastric ulcers would be the most proper form of therapy because of the high incidence of carcinoma of this type.

Answer: I fully agree with Dr. Stander's statement. Caution should be exercised in treating ulcers in the stomach by this method. During this series of cases I had a case of just such a circumstance. The stomach ulcer was large and of long standing. It was elected to do surgery and he was referred to the surgeon. A partial gastrectomy was done. The resected ulcer did not show any malignancy on section. In this particular case I feel now that the penicillin gastric drip would have been effective. Ten days more would not have harmed the patient any, and if a complete healing did not occur, operation could then have been undertaken.

**FOLLOW UP NOTE:** Since this paper was read July 16, 1947, 24 patients have been treated. Of the 24, 21 have been cured and three were failures. Of the three, one case passed kidney stones on the third day of treatment and it was necessary to discontinue treatment. The second patient became nervous and would not tolerate the tube in his stomach. The third patient developed penicillin rash on the third day of treatment. He was continued on the drip for five more days without penicillin, simply using a soda water. This was discontinued because of pain in the stomach and nausea. X-ray showed that there was no healing of the ulcer and indicated that soda water drip itself is not beneficial, answering in a way the question asked by Dr. J. E. Toups during the discussion.

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## THE USE OF CURARE IN TETANUS\*

E. ZOLLICOFFER BROWNE, M. D.†

AND

HARRY A. STONE, M. D.†

NEW ORLEANS

CASE REPORT

T. H. H., a white male, was first seen in the Emergency Room of the Southern Baptist Hospital

\*Presented at Staff Meeting of Southern Baptist Hospital on April 22, 1947.

†From the Staff of Southern Baptist Hospital, New Orleans, Louisiana.

in New Orleans on March 10, 1947 at 6 a. m., complaining of stiffness of the lower jaw; stiffness and soreness of the muscles of the neck, chest, back and abdomen; pain and soreness of right thumb. A history, obtained from his wife, revealed that he had stuck a splinter under cuticle of right thumb two weeks previously, while fishing. He removed what he thought was all of the splinter at that time, but received no medical attention for the injury. He had never been actively or passively immunized against tetanus. On March 8, 1947, stiffness in jaw muscles and difficulty in opening mouth first became apparent. The symptoms progressively grew worse and on the evening before admission marked stiffness and soreness in muscles of jaw, neck, chest and back ensued, with inability to open mouth more than a quarter of an inch. Some difficulty in swallowing was also noted.

*Physical examination* revealed a well developed, fairly well nourished white male, weighing about 150 pounds, appearing acutely ill, excited and apprehensive. There was marked rigidity of the muscles of the jaws and neck. Plainly in evidence was a typical "risus sardonicus." The abdomen was tense and rigid, but not tender on pressure. Opisthotonos was also noted. The distal phalanx of the right thumb was reddened and swollen on its dorsal aspect and showed a small area of supuration under mid-portion of cuticle. The temperature was 98.2°, pulse 95, respiration 26, blood pressure 142/80.

The *history* of a splinter stuck in the thumb—with no after care—the general physical findings and the symptoms presented made it fairly easy to rule out other pathologic conditions which must be considered—such as, meningitis, infection at root of third molar tooth, peritonsillar abscess, strychnine poisoning and tetany. So a diagnosis of tetanus was made and the patient was admitted to the hospital.

Immediately after his admission he was given skin and conjunctival tests for sensitivity to horse serum. These being negative, 100,000 units of anti-tetanus serum was given intravenously and 18,000 units into tissues of right thumb. Amytal gr. 11 was injected intravenously at this time. At 9 o'clock a. m., he was taken to operating room where a wood splinter 1.5 c.m. long was removed and the adjacent area of thumb widely opened and drained. Intravenous sodium pentothal, supplemented with nitrous oxide, was used for anesthesia. Three c.c. Intocostrin\* was given intravenously during the operation with marked relaxing effect on the generalized muscle spasm. It was decided then to continue the use of this drug and 1.5 c.c. was ordered to be given every four hours, either intravenously or intramuscularly, as best tolerated. This was done night and day until March 18, 1947 (eight days), when it was reduced to three times

\*The Squibb preparation of purified Chondrodendron tomentosum extract in aqueous diluent.



daily and continued thus until March 22. It proved to be very helpful and markedly reduced the use of sedatives and hypnotics. On one occasion an intravenous injection relaxed the patient so much that breathing was entirely by diaphragm and speech was extremely slurred. Prostigmin, as an antidote, and oxygen were kept immediately available, if respiration should become too markedly reduced. However, neither was used.

An additional 100,000 units A. T. S. intravenously was given at 3 p. m. of the day of admission and 50,000 units thereafter daily, intravenously, until March 17, when it was discontinued because of serum reaction. One intrathecal injection of 20,000 units was given on March 13. Penicillin was started the afternoon of admission with a dosage of 40,000 units intramuscularly every three hours and was continued until March 20, a total of 3,200,000 units. Benadryl, 50 mgm. t. i. d. was given from March 17 to 20.

*Laboratory Findings:* Urine was found to be negative, except for a faint trace of albumin and an occasional white blood cell and red blood cell. Blood picture showed 4,200,000 red blood cells; hemoglobin 12 gm. (83 per cent); total leukocytes 10,650; neutrophils 87 per cent, lymphocytes 7 per cent, eosinophiles 3 per cent, monocytes 3 per cent. Wassermann was negative. Blood chemistry: Total N. P. N., 39.3 mgm. per 100 c.c.; urea nitrogen, 14.7 mgm.; creatinine, 1.5 mgm.; uric acid, 2.0 mgm.; dextrose, 100 mgm. Spinal fluid: Negative. Sedimentation index, 14 mm. in 60 minutes.

*Course in Hospital:* The temperature remained normal until March 12 when it rose to 102° F. and remained elevated until March 16, when it returned to normal. A portable x-ray of the chest taken on March 15 was negative for pulmonary congestion.

The patient was delirious during the first four days and made several attempts to get out of bed. Once he fell but sustained no apparent injury except a small abrasion of the scalp. It was later discovered that he was attempting to jump from window as he thought he was going to die. He was given occasional doses of a barbiturate for sedation and narcotics as needed for pain. However, not much of these drugs were required, as above stated. A liquid diet was given until March 18 on account of inability to chew. The dressing on thumb was changed daily.

The patient gradually improved and on March 19 a diet was ordered as desired. He was allowed up in wheel chair on March 22. On this day he walked, but with much difficulty due to stiffness of the back. The ability to walk rapidly improved and he was discharged on March 24, 1947. At this time the infected thumb was almost healed.

#### CLINICAL DISCUSSION

Not overlooking the great value of tetanus antitoxin and barbiturates (and the questioned value of penicillin) in contributing to this recovery, I wish to stress the valiant role played by Intocostin, as I believe the patient would have died of exhaustion—due to the widespread massive spasm of his skeletal muscles, had we not had the relaxing effect secured by this drug. "The typical curare action" consists essentially of an interruption of nervous impulses to skeletal muscle at the myoneural junction. When Intocostin is introduced intravenously it rapidly produces a paralysis involving the skeletal muscles, the diaphragm and intercostals being last to be affected. The drug is excreted so rapidly that the duration of maximum effect is transient. This relaxing effect was a source of great relief to this patient undergoing massive spastic contraction. *Care and constant supervision of a patient receiving continuous relaxation, at or near, the level of respiratory paralysis is most important*, as experimental work indicates that the resultant hemoconcentration which apparently arises from loss of fluid from the vascular system into the relaxed muscles, may induce a state of shock. Adequate care in the amount of dosage and use of other measures to combat shock will materially lessen this danger, which after all, is certainly a lesser danger than would be faced if we did not have this drug in our armamentarium.

# NEW ORLEANS Medical and Surgical Journal

*Established 1844*

Published by the Louisiana State Medical Society under the jurisdiction of the following named Journal Committee:

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## THE STATE SOCIETY MEETING

The 68th Annual Meeting of the Louisiana State Medical Society will take place in Monroe on April 12-14. An attractive program has been prepared. The major portion of the first day, April 12, will be consumed by the two sessions of the House of Delegates. The business affairs of the Society and its relation to government interference require your earnest consideration. Important matters are to be reviewed at the several sessions.

It will be noted, by studying the tentative program in this issue, that the committee has followed the recent trend of grouping related subjects in symposia on April 13, the second day of the meeting. At the same time the needs of specialty groups have been met by arranging five sectional meetings, morning and afternoon, on Wednesday, the last day.

Of special interest will be the cancer symposium; hormone, tissue culture, hereditary and surgical features are being discussed in six concise papers. The symposium on medical diseases of the kidney will prove very interesting to the internist and to general practitioners.

The Society is fortunate in having ten guest speakers. They are:

Dr. Morris Fishbein, Chicago  
Dr. James Ernest Ayre, Montreal  
Dr. Ira T. Nathanson, Boston  
Dr. Harry S. N. Greene, New Haven  
Dr. J. E. Faber, Rochester, Minn.  
Dr. F. R. Lock, Winston-Salem  
Dr. Wm. F. Guerriero, Dallas  
Dr. Herbert Mantz, Kansas City, Mo.  
Dr. W. Ambrose McGee, Richmond  
Dr. George B. Eusterman, Rochester, Minn.

The program committee is to be congratulated on having arranged so inviting a program and it is anticipated that the members who attend will have a lively interest in the proceedings.

## STATE PROVISION FOR THE NATION'S HEALTH

The President of the United States, in his message to Congress on January 7, asked for "a national system of payment for medical care based on well tried insurance principles". In this section of the message and in the discussion of education the word "compulsory" was not noted. There was a request for an executive department or cabinet post for "health education and security". It may be expected, therefore, that other bills of the type typified by the Wagner-Murray-Dingell Bills will be forthcoming with the compulsory



feature submerged and the desirable change of a cabinet post for health will be offered. Efforts in the Congress to establish "state medicine" in some of its forms have been fought by the medical profession. After successive defeats the advocates of these bureaucratic experiments have changed the form in which the plan was presented. We anticipated, accordingly, a bill with some desirable or questionable features and many objectionable ones. It is necessary for the physicians to continue to be on the alert; to examine the proposals that are presented to Congress in any guise. We should acquaint ourselves and our patients with what others would like to put on them in the form of taxation, bureaucratic control, and professional embarrassment.

In 1917 the constitutional amendment allowing income taxes was quietly passed by the various theorists and social planners. The laws enacted under this amendment have grown. The regulations promulgated in accordance with such authority now con-

stitute volumes. As a result the affairs of income tax have become a concern of every individual under the flag. It affects every wage earner — bookkeeper, professional man, business man—everyone with an income. Every business policy or financial move has to be examined in the light of the income tax law. It will probably be found ultimately that the income tax will produce, in time, the panics in finance that our Federal Reserve Banking policies were designed to prevent. If the legislators who ratified the amendment 31 years ago had any idea of the extent of the effect of this law, the vast majority would have been afraid to approve it.

By the same token "health legislation", on a national scale, with or without the word compulsory, bears the same threat. As practitioners of medicine we have our freedom now. We also have the power to oppose being regimented. The statement which came down from one of the founders of our Country; "The power to tax is the power to destroy", was never more true than now.

# TENTATIVE PROGRAM

## 1948 ANNUAL MEETING—FRANCES HOTEL—MONROE

### MONDAY, APRIL 12

#### ROOF

9:00 A. M.	House of Delegates
Luncheon	House of Delegates
2:00 P. M.	House of Delegates
8:00 P. M.	General Public Meeting
	1. *Morris Fishbein, M. D., Chicago
	2. Cytologic Diagnosis of Cancer—James Ernest Ayre, M. D., Montreal
	*Subject to be announced

### TUESDAY, APRIL 13

#### ROOF

9:00 A. M.	<b>Symposium on Cancer:</b> Ambrose Storck, M. D., New Orleans
	1. The Influence of Sex Hormones and Castration on Advanced Cancer of the Breast and Prostate—Ira T. Nathanson, M. D., Boston, Mass.
	2. The Incidence and Management of Lymph Node Involvement in Cancer—Ira T. Nathanson, M. D., Boston, Mass.
	3. Clinical Application of In Vivo Tissue Culture—Harry S. N. Greene, M. D., New Haven, Conn.
	4. Recent Advances in the Treatment of Carcinoma of the Cervix and Fundus—E. Perry Thomas, M. D., New Orleans
	5. Genetics and Cancer—Walter J. Burdette, M. D., New Orleans
	6. Carcinoma of the Colon and Rectum—S. A. Romano, M. D., L. H. Kuker, M. D., and C. C. Craighead, M. D., New Orleans
Luncheon	General Membership
2:00 P. M.	* <b>Symposium—Medical Diseases of the Kidney:</b> Samuel B. Nadler, M. D., New Orleans
	*Subjects to be announced
8:00 P. M.	President's Reception

### WEDNESDAY, APRIL 14

9:00 A. M.

#### ROOF

House of Delegates

#### ROOM A

**Obstetrics:** R. B. Wallace, M. D., Alexandria

1. Clinical Experience with the Rh Factor in Obstetrics—E. L. King, M. D., and John A. King, M. D., New Orleans
2. Management of Premature Labor—C. J. Lund, M. D., New Orleans
3. Experiences with Anti-Coagulants in Postpartum Patients—J. E. Faber, M. D., Rochester, Minn.
4. Maternal Mortality in the South—F. R. Lock, M. D., Winston-Salem, N. C.

**Gynecology:** Conrad G. Collins, M. D., New Orleans

1. Some Clinical Considerations on the Sterility Problem from the Viewpoint of the Gynecologist—B. B. Weinstein, M. D., New Orleans
- Discussion—C. R. Mays, M. D., Shreveport
2. Retrodisplacements of the Uterus—Peter Graffagnino, M. D., New Orleans
- Discussion—Howard P. Hewitt, M. D., Lafayette
3. Menopausal Bleeding—C. H. Tyrone, M. D., New Orleans
- Discussion—R. E. C. Miller, M. D., Alexandria
4. Gyn-Like Complaints—Wm. F. Guerriero, M. D., Dallas, Texas
- Discussion—Jack R. Jones, M. D., Baton Rouge

#### ROOM B

**Medicine:** M. W. Hunter, M. D., Monroe

1. Drugs of the Present and Future—P. M. Tiller, Jr., M. D., New Orleans
2. Gastroscopy—Carl Rabin, M. D., New Orleans
- Discussion—Felix J. Willey, M. D., New Orleans
3. Unusual Manifestations of Coronary Heart Disease—T. H. DeLaurel, M. D., Lake Charles
- Discussion—Manuel Gardberg, M. D., New Orleans
4. Modern Advances in Diabetes Mellitus—Frank W. Pickell, Jr., Baton Rouge
5. Treatment of Acute Brucellosis—T. B. Tooke, Jr., M. D., Shreveport

**Orthopedics:** Geo. C. Battalora, M. D., New Orleans

1. Specific Treatment of the Fractured Ankle—Irving Redler, M. D., New Orleans

#### ROOM D

**Radiology:** John M. Miles, M. D., Lafayette

1. \*D. D. Moore, Monroe

**Neuropsychiatry:** Walter J. Otis, M. D., New Orleans

1. Psychosomatic Problems in Adolescents—Herbert E. Harms, M. D., New Orleans
2. Psychiatric Emergencies—Max Johnson, M. D., New Orleans

**Public Health:** Wm. M. Johnson, M. D., Leesville

1. Diagnosis of Tuberculosis—Herbert Mantz, M. D., Kansas City, Mo.
2. Ignorance is Not Bliss—M. P. Martin, M. D., New Orleans

\*Subject to be announced

(Continued on Next Page)



(Continued from preceding page)

**ROOM 210**

- Bacteriology and Pathology:** Edwin H. Lawson, M. D., New Orleans
1. Human Equine Encephalomyelitis (Eastern Type) in Louisiana—George H. Hauser, M. D., New Orleans
  2. Encephalomyelitis (Eastern Type) Occurring in Horses and Mules in Louisiana—E. P. Flower, D. V. S., Baton Rouge
  3. Causes and Prevention of Transfusion Reactions—J. W. Davenport, M. D., New Orleans
  4. Pathology of Transfusion Reactions—S. H. Colvin, M. D., New Orleans
- Eye:** Wm. B. Clark, M. D., New Orleans
1. The Role of Early Retrobulbar Neuritis in Management of Senile Cataracts—Shelley R. Gaines, M. D., New Orleans

**Luncheons**

- |                             |  |
|-----------------------------|--|
| Obs. & Gynecology           | Tuberculosis-Histoplasmosis in La.—    |
| Medicine                    | Herbert Mantz, M. D., Kansas City, Mo. |
| Orthopedics—no luncheon     | Pediatrics—no luncheon*                |
| Radiology                   | Allergy—no luncheon                    |
| Neuropsychiatry—no luncheon | Dermatology—no luncheon                |
| Public Health               | Urology                                |
| Bacteriology and Pathology  | Surgery—no luncheon                    |
| Eye—no luncheon             | Gastro-enterology                      |
|                             | *Dinner                                |

2:00 P. M.

**ROOM A**

- La. Tuberculosis Assn.:** Sydney Jacobs, M. D., New Orleans
1. Some Data Pertinent to the Diagnosis and Prognosis of Pulmonary Tuberculosis—Philip B. Johnson, M. D., and Louis A. Monte, M. D., New Orleans
  2. X-ray Diagnosis of Pulmonary Tuberculosis—J. E. Blum, III, M. D., Greenwell Springs
  3. Collapse Therapy in the Treatment of Tuberculosis—Dewey L. Anderson, M. D., Monroe
  4. Recent Trends in the Surgery of Pulmonary Tuberculosis—Louis F. Knoepp, M. D., Shreveport
  5. Streptomycin in the Negro with Tuberculosis—Nathan Goldstein, M. D., New Orleans
  6. X-ray Conference—Maurice Campagna, M. D., New Orleans

**ROOM B**

- Pediatrics:** R. V. Platou, M. D., New Orleans
1. Clinical Features of a Summer Epidemic Disease (Three Day Fever)—Clarence H. Webb, M. D., and S. George Wolfe, M. D., Shreveport
  2. Epidemiological Studies on Three Day Fever—Verre Simpson, M. D., Shreveport
  3. Postgraduate Education in Pediatrics for General Practitioners—Sidney S. Chipman, M. D., New Orleans
  4. Kerosene Poisoning—N. Bologna, M. D., and N. Woody, M. D., New Orleans
  5. Advantages of Early Recognition and Treatment of Allergic Disorders of Infancy and Childhood—W. Ambrose McGee, M. D., Richmond, Va.
  6. Diagnosis at a Glance—Conway S. Magee, M. D., Lake Charles

**ROOM D**

- La. State Allergy Society:** B. G. Efron, M. D., New Orleans

**CASE REPORTS:**

1. Contact Dermatitis—Henry D. Ogden, M. D., New Orleans  
Discussion—R. E. Selser, M. D., Baton Rouge
2. Treatment of Asthma with Isuprel—H. Whitney Boggs, M. D., Shreveport  
Discussion—Dewey L. Anderson, M. D., Monroe
3. Provocative Test in Hypersensitivity—Stanley Cohen, M. D., New Orleans  
Discussion—B. G. Efron, M. D., New Orleans
4. Possible Allergy in Dermatomyositis—W. H. Browning, M. D., Shreveport  
Discussion—J. Dudley Youman, M. D., Shreveport
5. Purpura Due to Allergy—B. G. Efron, M. D., New Orleans  
Discussion—Vincent J. Derbes, M. D., New Orleans

**ROOM 210**

- Dermatology:** Medd Henington, M. D., New Orleans
1. Eruptions of the Hands and Feet and Their Treatment—Barrett Kennedy, M. D., New Orleans
  2. The Treatment of Certain Dermatoses with Oral Bismuth—J. K. Howles, M. D., New Orleans
- Urology:** DeWitt T. Milam, M. D., Monroe
1. Modern Treatment of Urinary Tract Infections—Hugh T. Beacham, M. D., New Orleans
  2. Retropubic Prostatectomy (moving picture)—R. K. Womack, M. D., Shreveport.

**ROOF**

- Surgery:** J. D. Rives, M. D., New Orleans
1. Decortication of the Lung—Walter W. McCook, Jr., M. D., Shreveport
  2. Combined Abdomino-Thoracic Injuries—Donald B. Williams, M. D., Lafayette
  3. Vascular Injuries—Paul D. Abramson, M. D., Shreveport
  4. The Pre and Postoperative Management of the Substandard Surgical Risk—Champ Lyons, M. D., New Orleans
- Gastro-enterology:** T. B. Tooke, Jr., Shreveport
1. Penicillin in Treatment of Peptic Ulcer—R. W. Young, M. D., Baton Rouge
  2. Newer Aspects of the Management of the Peptic Ulcer Patient—George B. Eusterman, M. D., Rochester, Minn.
  3. Round Table Discussion—Vagotomy: Its Surgical and Medical Aspects—George B. Eusterman, M. D., Rochester, Minn.; Gordon McHardy, M. D., New Orleans; Howard R. Mahorner, M. D., New Orleans; R. M. Penick, Jr., New Orleans

## MISSOURI PACIFIC LINES

## New Orleans-Monroe

Leave New Orleans 8:30 p. m.—Arrive Monroe 4:25 a. m. (Set out sleeper until 8 a. m.)

Leave Monroe 11:50 p. m. (Sleeper open 9:30 p. m.)—Arrive New Orleans 7:59 a. m.

Round trip first class fare.....	\$19.21
Pullman fares each way: Lower berth.....	4.03
Upper berth.....	2.99
Drawing room (2 or more).....	14.15
Exclusive Pullman occupancy.....	86.60

In the event a sufficient number make the trip to justify doing so, extra Pullman equipment will be made available. If additional information is desired communicate with Mr. J. T. Leze, Passenger Department, Missouri Pacific Lines, New Orleans.

## ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

***An informed profession should be a wise one.***

## INTERIM MEETING

## A. M. A. HOUSE OF DELEGATES

Members of Executive Committee  
Louisiana State Medical Society  
1430 Tulane Avenue  
New Orleans 13

Gentlemen:

Following is a report of the interim meeting of the American Medical Association House of Delegates held on Monday and Tuesday, January 5 and 6, 1948 in Cleveland, Ohio. Dr. Graves and I, Delegates to the meeting, thought it would be interesting to the members of our State Society to know just what has taken place at this meeting and hence this report.

The meeting was called to order shortly after ten A. M. by the Speaker of the House, Dr. R. W. Fouts, of Omaha, Nebraska. The Chairman of the Reference Committee on Credentials reported 138 accredited delegates. The Speaker then announced the appointment of his committees and Dr. Graves was appointed to the Elections Committee and I was appointed to the Committee on Sections and Section Work.

The names of three general practitioners were then submitted for the General Practitioner's Award. The final vote showed that Dr. A. C. Sudan, of Colorado, received a majority vote on the first ballot and he was designated the winner of the medal.

Remarks of the President and President-elect and report of officers and committees was the next order of business. Following this adjournment took place until two-thirty in the afternoon, when reports were received.

The first report was a very lengthy one by the Committee to Expedite Work of the House of Delegates. Since the Annual Meeting covers four full days and the Interim Meeting only two days a complete agenda for both meetings was presented and adopted. There is no need to burden you with the order of business of these two different sessions as I am sure they will appear in the Journal of the A.M.A.

A uniform method of electing delegates was decided upon. This new system is the one used by the Louisiana State Medical Society so there will be no change in our present method of election of delegates.

Recommendation was adopted that it be a standing rule that the Speaker of the House appoint reference committees two months in advance of a session and that the list of appointments be published one month in advance of the session. This is in contradiction to what is being done at the present when the Speaker of the House announces the committees as the first order of business.

There was a rather controversial discussion of just what an executive session of the



House means and this was clarified to the satisfaction of all of the delegates.

The Committee on the Constitution and By-Laws has almost finished its extensive work and the committee feels sure that it will be able to submit its final draft at the June meeting in Chicago.

There was some discussion about the time of the Interim meeting this year since it was held when thousands of college and school students were on their way back from the Christmas holidays. It was decided that the usual time for the Interim Meeting would be in the month of December unless accommodations can not be obtained; under such conditions the decision will be left to the Board of Trustees.

It was brought out that the A.M.A. worked with a deficit of over \$100,000.00 during the past year and a recommendation was made and passed that the dues for 1948 should be increased to \$12.00. After this year the Board of Trustees will have the authority to raise the dues to any amount not exceeding \$12.00.

A Committee from the A.M.A., the American Hospital Association and the American Nurses Association, consisting of fifteen members, was recommended; this committee to be known as "a coordinating committee for the study of nursing problems".

Approval was given for the formation of a Committee on Multiple Sclerosis Program of Education.

A committee was appointed to study the formation of regulations governing rotating internships in hospitals before a doctor is permitted specialty training. This committee is also to formulate plans to staff hospitals with interns by limiting the number of interns to the bed capacity of the hospital. This will be a committee of five, two of whom are to be general practitioners, and the committee is to report at the Annual Meeting in June. They are also to stress the formation of a Residency of general practice in hospitals.

A classification of medical students in some form of membership in the A.M.A. is now under consideration.

Dr. Bortz complimented the work of the Woman's Auxiliary and exhorted the delegates to organize such auxiliaries in states where none are present.

Case findings with x-ray have produced such great results in finding of tuberculosis that the A.M.A. will endeavor to further measures to make as widespread as possible the dissemination of this information and it was agreed that complete physical examination, including x-rays of the chest would be required of all immigrants before they are admitted to this country.

A resolution limiting the term of delegates was *not* approved.

Another resolution asking for a better geographical distribution of the Board of Trustees failed to pass.

The so-called exploitation of the x-ray and pathological departments by hospitals was referred to a new committee that is to be appointed to study this problem and to report at the June meeting.

The brochure as presented by the Committee on Rural Medical Service was distributed and the committee was congratulated for the excellent work it has accomplished. We were pleased to see the excellent report from the Chairman of our State Committee in this brochure.

The reference committee to study the Blood Bank of the Red Cross approved again, in principle, the establishment of blood banks by the American Red Cross provided that the American Red Cross accept the following principle: To insure safety to recipients, the responsibility for technical details must rest on properly trained personnel under the control of local or state medical societies. The committee further recommends that the American Red Cross be asked to accept a permanent committee from the A.M.A. to coordinate the medical work of the Red Cross.

It was reported that the News Letter is now being sent to approximately 3500 practicing physicians in the United States and that any doctor who desires to receive this can apply to the A.M.A. to be placed on the mailing list.

It was brought out that any prepayment medical plan, whether profit or non-profit, if it is acceptable to the county or state medical society, may apply for recognition in the Associated Medical Care Plans, however they must meet certain requirements before being accepted. No doubt you have seen in the newspapers of Sunday, January 11, that General Hawley, former director of the medical services of the Veterans Administration, will be the coordinator or director of a combined committee of the Blue Cross Commission and Associated Medical Care Plans.

The interim session adjourned on Tuesday afternoon at four-thirty.

On Monday evening at seven o'clock a joint dinner of the delegates was held with the members of the Council on Industrial Health, sponsored by the Cleveland Chamber of Commerce and the Cleveland Aca-

demy of Medicine. This was a very interesting meeting with some excellent motion pictures of atom bomb destruction at Bikini. Also a patient was brought over from New York and demonstrated as an example of what can be accomplished by rehabilitation training. This was a young man who had suffered from poliomyelitis and both arms and both legs were involved.

Dr. Graves received the assurance of Dr. Morris Fishbein that he will attend and address the Annual Meeting of the Louisiana State Medical Society in Monroe.

If there is any further information any member of the Executive Committee desires I am sure Dr. Graves or I will be glad to furnish whatever we can.

Respectfully submitted,

VAL H. FUCHS, M. D.,  
Delegate.

## LOUISIANA STATE MEDICAL SOCIETY NEWS

### C A L E N D A R

#### PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

#### PUBLIC RELATIONS PROGRAM ANNOUNCED BY COUNCIL

The public relations program for the year 1948 was announced recently by Dr. A. V. Friedrichs, Chairman of the Council on Medical Service and Public Relations and will be mailed to all members of the State Society.

The purpose of this program shall be to further a better understanding of problems common both to the laity and the profession, to disseminate information which is of general interest and value to keep both the public and the medical profession informed of significant progress in the field of public relations.

The program is to be promulgated under the leadership of the Council on Medical Service and Public Relations in cooperation with the Executive

Committee and the House of Delegates of the Louisiana State Medical Society, and is to serve as a guide-post to component parish medical societies and their respective committees.

The public relations program is composed of the following projects:

1. Professional Relations between Physicians.
2. Professional Relations with Allied Professions and Auxiliary Groups.
3. General Public Relations.
4. Promotion of Voluntary Health Insurance.
5. Relations with Civic Agencies and Societies.
6. Relations with Government Agencies.
7. Relations with Civic Clubs.
8. Relations with Molders of Public Opinion.
9. Patient-Physician Relations.
10. Public Relations in Rural Health.



11. Assist in Establishing Health Councils.
12. Miscellaneous.

The Council has an overall program proposed which will take quite some time to develop in its entirety. There are a number of important phases associated with the Council's program, especially under the heading of "general public relations", and it is proposed to establish ultimately an active News Bureau and through this medium keep the general public properly informed of news pertaining to the medical profession.

Another important phase of the program is the establishment of Health Radio programs throughout the State of Louisiana on as many radio stations as it is possible to secure time as a public service feature. One radio program has already been started and within a short time a number of other programs will be announced. It is also proposed that a Speakers' Bureau be established both on a statewide basis and on a parish or community basis. Through the medium of this Bureau, speakers will be made available to civic clubs, women's clubs, political rallies, government hearings, and on all occasions when a prominent speaker is necessary to discuss such subjects as voluntary health insurance, compulsory health insurance, health, physical and safety education, public health, the operations of a medical society, socialized medicine, and numerous other subjects of public interest.

The cooperation of every component medical society will be needed to successfully present this public relations program. The Woman's Auxiliary to the various parish medical societies can be of great value to the Council in assisting it in fulfilling its objective.

A copy has been mailed to every member of the Louisiana State Medical Society and we ask that you review same and keep it in your files for future use. You will see that it contains many phases in which each member of the medical profession can actively participate. Your wholehearted cooperation in its presentation and fulfillment will be your answer to offset the government's cry for socialization of medicine.

#### PUBLIC RELATIONS COUNCIL STARTS FIRST BROADCAST

The first of a series of broadcasts, presented by the Council on Medical Service and Public Relations of the Louisiana State Medical Society in cooperation with the Ouachita Parish Medical Society and its Woman's Auxiliary, was presented on Wednesday, January 14 over Radio Station KNOE in Monroe. The series consists of 13 weekly broadcasts of 15 minutes each and is entitled "Before the Doctor Comes".

The series is a practical, reassuring group of interviews in which the mother asks the doctor what

to do about her everyday health problems. The series tells what to do "Before the Doctor Comes" in case the patient is suffering from sniffles, sore throat and coughs, fever, rash, headache, earache, or in cases suffering from bad bumps or other accidents. Radio Station KNOE in Monroe has donated this time as a public service feature to the Council on Medical Service and Public Relations.

The broadcasts will be from transcriptions prepared by the American Medical Association. Material is from the library and publications of the A.M.A. Numerous eminent physicians, both in medical practice and public health work, have been brought before the microphone to be interviewed. All scripts are professionally prepared by experienced radio writers and the voice of the interviewer is that of Harriet Hester, formerly of the staff of WLS of Chicago, well-known NBC interviewer. Harriet Hester and William J. Murphy, veteran writer of medical scripts, have written the continuity. In the musical portion of the program, Elwyn Owen is at the organ.

The preparation of the series is under the general direction of Dr. W. W. Bauer, Director of Bureau of Health Education of the American Medical Association, who appears on the program and his associate in the bureau, Dr. William W. Bolton. The broadcast was made possible through the wholehearted cooperation of Mr. R. W. Dumm, General Manager of KNOE.

Members of the Public Relations Committee of the Woman's Auxiliary to the Ouachita Parish Medical Society assisted in the arrangements and presentation of the broadcast in that area. Members of the committee are Mrs. H. B. Collins, Chairman; Mrs. C. B. Flinn; Mrs. C. P. Gray, Jr.; Mrs. Hayden Cutler; and Mrs. J. E. McConnell.

#### HEALTH BROADCASTS NOW AVAILABLE TO PARISH SOCIETIES

Series of transcribed health broadcasts are now available and may be presented by the parish medical societies in cooperation with the Council on Medical Service and Public Relations of the Louisiana State Medical Society, Frank Lais, Jr., Executive Director of the Council announced recently.

The programs are of a 15-minute duration to be presented weekly and will be furnished to any radio station selected by the parish medical society, at no cost to the station or the society. All organizations interested in presenting a series of health broadcasts in their community should contact the office of the Council, Room 103, 1430 Tulane Avenue, New Orleans, Louisiana.

#### WHAT OTHER STATES ARE DOING IN REGARD TO PUBLIC RELATIONS

After a meeting of the Virginia Medical Public Relations Conference, held in Richmond, Virginia,

on December 20, a report was prepared by Frank Lais, Jr., Executive Director of the Council on Medical Service and Public Relations.

We thought it would be interesting to know what some of the other states are doing in public relations and also some of the comments made by persons closely associated with the medical profession.

Dr. Walter B. Martin of Norfolk, Virginia, member of the Council on Medical Service of the A.M.A., spoke on benefits of medical care under a voluntary system. He paid a particular compliment to the Southern Regional Conference held in New Orleans and expressed the desire for semi-annual conferences such as the one held and also commented on the value of the conferences held in Atlanta and Philadelphia. He advised the group that it was through this medium that the A.M.A. is bringing information to the individual state societies. He stated that the A.M.A. District Councils have been organized and that the A.M.A. will use the Councilors as contact men. He stated that the A.M.A. cannot formulate an overall program of medical care that will satisfy all sections of the country—all plans should be formulated on a district or local basis and that public opinion should be developed in the local areas.

He stated that the A.M.A. can only be used to formulate policies and evaluate certain principles, and that the implementation of any program must go back to the individual state societies. He strongly recommended the formation and organization of state, parish and local health councils—health councils should include lay individuals and representative citizens. The council should be composed of 15 or 20 individuals including two or three doctors. He stated that doctors should not dominate the council or try to control it but should take leadership in the operation. He stated that the council should be an influence on the type of medical care that is available, and should not be organized on the basis of personal gain for individuals. They should be impressed as to the advantages of good medical care and also why certain practices such as that of chiropractors and naturopaths are not acceptable.

He cautioned members about sidetracking such programs as the V.A. program and the Coalminers Medical Care. He stated that the coalminers program may include 16 to 20 million people, and 50 to 60 million persons, including veterans and their dependents, will ultimately be covered by the V.A. program. He stated that if such programs are carried out on an individual basis, it would eliminate a large quantity of medical care from the community and he urged all doctors to cooperate with these services to keep them on a local basis. If this is not done on a community basis, large groups will be organized on a national basis and little will be left on an individual basis.

Dr. J. M. Emmett, Chairman of the Public Relations Committee of the Medical Society of Virginia, stated if doctors do not assume the responsibility of the distribution of medical care, then the Federal Government will take over the provision of this care. Doctors should not however dominate the local health councils and should use lay individuals to assist them in the local health councils. The interest of adequate medical care is being sponsored by too small a group of individual doctors and he urged more doctors to become interested in the promotion of adequate medical care. Adequate medical care must be presented by large groups of doctors and a small group of standard-bearers should not be forced to carry the load.

He stated that an attempt to tell the people that the practice of medicine is perfect, is wrong, because it is not perfect. It is doubtful that the public believes that medicine as it is today is on an adequate basis. The system is as far advanced as a group can go individually. Surely, there is no better way than to keep medicine as a private practice but the secret is to get the people who believe as do the doctors to associate with them.

Dr. H. B. Mulholland, a member of the Public Relations Committee and Assistant Dean of the University of Virginia Medical School, stated that the people are now interested in adequate medical care and that much of the need for medical care has come out of Washington rather than from the doctors themselves. Doctors have been more interested in the delivery of medical care than in seeing that all have adequate medical care.

Doctors must show the people—even though the doctors provide adequate facilities, the people must be educated to use these facilities and shown how to use them when they are available. He suggested that this be started in the schools and that doctors must be leaders in their community in the organization of health councils. The doctor must discuss his problems with other leaders and he should be particularly informed on the availability of prepayment medical care insurance because most people are interested in acquiring health insurance.

Dr. L. J. Roper, a member of the Public Relations Committee and Commissioner of Health for the State of Virginia, stated that the relationship of public health services and the doctors depends upon the cooperation of both groups. The relationship between the two groups is broadening considerably throughout the nation. Both are working harmoniously in Virginia. He stated that his public health department has implemented a program for cancer and for other services far ahead of the old public health program. He stated that there was a time when the relationship between the two groups was not too good but now the differences have been adjusted.

The public health program of Virginia utilizes the services of physicians and physicians are al-



ways willing to help. He said the public health service now uses the services of all physicians in the examination of school children.

Health officers in Virginia are the friends of the doctors and it is their desire to cooperate in every way. The public health doctor in Virginia is considered as a "wholesaler" because he deals with the masses, and the individual doctor is the "retailer" of medical services because he deals with the individual.

Dr. William Shands Meacham, Director of the Virginia Council on Health and Medical Care, spoke on the organization of health councils on a state, county, and community basis in Virginia. The health council in Virginia is organized on an incorporated basis, separate from any particular organization. All of the health councils are supported by voluntary contributions from all cooperating government agencies, the medical societies, and other interested individuals.

Dr. W. R. Pretlow, President of the Virginia Medical Service Association (the Virginia prepayment medical care plan), advised the physicians present that it is up to the doctors in their individual state to do something for the people who are in need of medical care or the government is going to do it. He does not believe that talking to Congressmen, talking to your nextdoor neighbor, articles in the newspapers about the fallacies of socialized medicine are sufficient. These will offer only temporary relief and the medical profession will still be in a state of emergency.

The only assurance against socialized medicine is for the doctors to get behind their voluntary prepayment insurance plans and actively promote them so that people will be protected, and then, and only then, will there be an answer to the government's demand.

People will feel the need for medical care plans during the next depression and the doctors should get behind the plans to enroll everyone. He earnestly recommends the inclusion of promotional literature in the monthly bills of each physician.

The most enlightening and constructive paper of the day was delivered by Dr. John T. Hundley, a member of the District Council—Lynchburg Academy of Medicine. Dr. Hundley conducted an individual survey to determine the attitude of a selected group of individuals toward the medical profession. The survey included newspaper editors, union leaders, bankers, lawyers, persons in every walk of life, rich and poor, persons who are confined to some of their charity institutions. The survey asked that these individuals list any grievance of which they have knowledge pertaining to the medical profession. His survey was startling and members in attendance were wide-eyed as he read some of the comments from his survey.

The survey prepared by Dr. Hundley is to be mimeographed and possibly reproduced in the A.M.A. Journal.

Dr. Guy Fisher, President of the Medical Society of Virginia, in closing the meeting, stated that the humanitarian spirit of medicine is lacking and that is one reason why the laity is doubting the medical profession.

#### ORGANIZATION OF HEALTH COUNCIL

Citizens of Lake Providence recently met in the courthouse for the purpose of organizing a permanent health council. The meeting was called in cooperation with the East Carroll Parish Farm Bureau and the Council on Medical Service and Public Relations of the Louisiana State Medical Society. About two hundred persons attended the meeting and unanimously endorsed the organization of a permanent health council in East Carroll Parish. Dr. Forrest M. Terral of Lake Providence was elected permanent chairman of the East Carroll Parish Health Council.

Dr. John Snelling of Monroe represented the Council on Medical Service and Public Relations and talked on the advantages to be obtained through the organization and establishment of a health council. Also attending the meeting were Frank Lais, Jr., Executive Director of the Council on Medical Service and Public Relations and Mr. P. A. Colvin of Monroe, who explained the advantages of voluntary health insurance. Also appearing on the program were Mrs. T. R. Tomlinson, Chairman of the Louisiana Rural Health Council, and Miss Mary Mims, State Extension Sociologist.

A representative from the department of Institutions also appeared before the council and interested the group in the construction of a hospital in the Lake Providence area.

#### NEW OFFICERS OF COMPONENT SOCIETIES

The following officers have been elected by their respective parish societies to serve for 1948.

##### Avoyelles Parish Medical Society—

President—Dr. James Knoll, Bunkie  
Vice-Pres.—Dr. Philip P. Giuffre, Cottonport  
Sec.-Treas.—Dr. S. R. Abramson, Marksville  
Delegate—Dr. Kirby A. Roy, Mansura

##### Beauregard Parish Medical Society—

President—Dr. John D. Frazar, DeRidder  
Vice-Pres.—Dr. Luke M. Marcello, DeRidder  
Sec.-Treas.—Dr. Sam T. Roberts, DeRidder  
Delegate—Dr. John D. Frazar, DeRidder  
Alternate—Dr. Luke M. Marcello, DeRidder

##### Claiborne Parish Medical Society—

President—Dr. S. A. Tatum, Homer  
Vice-Pres.—Dr. J. E. Batchelor, Haynesville  
Sec.-Treas.—Dr. Martin L. Forcht, Haynesville  
Delegate—Dr. Thomas M. Deas, Homer  
Alternate—Dr. J. W. Featherston, Homer

##### DeSoto Parish Medical Society—

President—Dr. W. B. Hewitt, Mansfield

Vice-Pres.—Dr. R. P. Thaxton, Mansfield  
 Sec.-Treas.—Dr. R. A. Tharp, Mansfield  
 Delegate—Dr. R. A. Tharp, Mansfield

#### Franklin Parish Medical Society—

President—Dr. W. L. Strahan, Winnsboro  
 Vice-Pres.—Dr. John N. Bostick, Gilbert  
 Sec.-Treas.—Dr. A. J. Reynolds, Winnsboro  
 Delegate—Dr. H. T. Rogers, Winnsboro

#### Jackson-Lincoln-Union Parish Medical Society—

President—Dr. Carl F. Langford, Ruston  
 Vice-Pres.—Dr. T. D. Boaz, Jonesboro (Jackson)  
 Dr. W. P. Lambeth, Farmerville  
 (Union)

Sec.-Treas.—Dr. John A. Thomas, Ruston  
 Delegate—Dr. T. A. Dekle, Jonesboro  
 Alternate—Dr. M. T. Green, Ruston

#### Jefferson-Davis Medical Society—

President—Dr. Morgan Smith, Jennings  
 Vice-Pres.—Dr. John G. McClure, Welsh  
 Sec.-Treas.—Dr. L. E. Shirley, Jennings  
 Delegate—Dr. John G. McClure, Welsh  
 Alternate—Dr. F. W. Harrell, Jennings

#### St. Landry Parish Medical Society—

President—Dr. F. O. Pavy, Leonville  
 Vice-Pres.—Dr. Charles W. Lewis, Eunice  
 Sec.-Treas.—Dr. C. L. Mengis, Opelousas  
 Delegate—Dr. F. Creighton Shute, Opelousas  
 Alternate—Dr. S. J. Rozas, Opelousas

#### St. Mary Parish Medical Society—

President—Dr. T. H. Gueymard, Morgan City  
 Vice-Pres.—Dr. C. R. Brownell, Morgan City  
 Sec.-Treas.—Dr. S. J. Russo, Morgan City

#### Vernon Parish Medical Society—

President—Dr. Joe E. Broyles, Leesville  
 Vice-Pres.—Dr. E. H. Byrd, Leesville  
 Sec.-Treas.—Dr. William M. Johnson, Leesville  
 Delegate—Dr. William M. Johnson, Leesville  
 Alternate—Dr. M. W. Talbot, Leesville

### RESIDENT NEEDED

Information has been received that there is need at this time for a part time resident at the Metairie Hospital in New Orleans. For further information contact the Secretary of the Hospital, Mr. J. Strauss, 310 Codifer Boulevard, New Orleans.

### NEW ORLEANS ACADEMY OF INTERNAL MEDICINE

The newly formed New Orleans Academy of Internal Medicine held its first dinner meeting on Thursday, January 15, 1948.

Following a short business meeting and dinner, the guest speaker, Dr. Robert Nieset, delivered the address. His subject was "Some Relations of Modern Physics to Medical Research". Dr. Nieset is Director of Biophysics Research at Tulane University.

The officers of the new organization are Dr. Thomas Findley, President; Dr. Willard Wirth, Vice-President; Dr. Sam Nadler, Secretary-Treasurer, and Dr. Edgar Hull and Dr. Chaille Jamison, additional members of the Executive Committee.

The next meeting of the Academy will be some time in April, to be announced later.

### APPOINTMENT OF COMMISSIONED OFFICERS IN THE MEDICAL CORPS AND DENTAL CORPS OF THE REGULAR NAVY

The statutory authority contained in Public Law 365—80th Congress, Title II (Army-Navy-Public Health Service Medical Officer Procurement Act of 1947) makes it possible now for civilian doctors to become commissioned officers in the regular Navy, provided they meet the professional and physical qualifications. This law is unique in that it does away with, for the first time, the age limitation of thirty-two years of age and permits doctors in civilian practice to enter the Navy and be commissioned with the rank up to and including Captain. The law considers all strata of the medical profession, internes, residents, reserves, former medical officers who have resigned, and present practicing physicians.

In order to make application a doctor must be a citizen of the United States, a graduate from a Class "A" medical school and have served at least one year's internship in an approved hospital. Candidates will then be judged on a number of qualifications such as being a member of a specialty board, his teaching connections, the number of years of professional or scientific practice, hospital or laboratory connections, a statement of military service, etc.

The allocation of rank to successful candidates will depend upon their academic age, professional standing, and experience in the medical field. Successful candidates will then be integrated in line with medical officers of the regular Navy and assigned running mates accordingly. This means that they will be eligible for promotion along with their fellow officers of equal rank.

This law offers a fine opportunity for civilian doctors to make a career in the regular Navy and to enjoy its professional advantages as well as its retirement benefits. Doctors interested in such a career should write to the Bureau of Naval Personnel, via the Bureau of Medicine and Surgery, Navy Department, Washington, D. C.

### NEW HOSPITAL

The organizational meeting of the staff of the new Physicians & Surgeons Hospital at Shreveport was held on December 12, 1947, after a dinner in the Physicians and Surgeons Cafeteria, with thirty-nine members in attendance. Dr. J. R.



Stamper was elected president, Dr. W. S. Harmon, vice-president, and Dr. Joe E. Holoubek, secretary. An executive committee consisting of Dr. L. W. Gorton, Dr. Wallace Brown and Dr. Keith Mason was appointed and will draw up the by-laws and constitution of the staff.

The Physicians & Surgeons Hospital is a new 106 bed hospital constructed under the guidance of Dr. J. R. Stamper near the Physicians & Surgeons Building. The architecture is modernistic in design, the building is completely air-conditioned and is so constructed that expansion will be easily made.

The staff of the Physicians & Surgeons Hospital is open to physicians who are members of the local and state medical societies.

#### GORDON MORGAN

1867-1948

Dr. Gordon Morgan, of Melville died on January 20. Dr. Morgan had been an active member of the State Society since 1915 and at the time of his death was Vice-President of the St. Landry Parish Medical Society.

#### WOMAN'S AUXILIARY, LOUISIANA STATE MEDICAL SOCIETY

The National Federation of Small Business, Inc., is sponsoring radio broadcasts on socialized medicine. So far there have been two discussions made by them over the radio on this subject. This is of particular interest to the Woman's Auxiliary to the Louisiana State Medical Society and ma-

terial for distribution or information may be had by writing to: National Federation of Small Business, Inc., San Mateo, California. These pamphlets are splendid and were especially written to be read from coast to coast, so we urge you to get this material as we are sure you will find it of invaluable aid.

To emphasize the importance of these forceful talks, we quote the last paragraph of the second discussion:

"Through these broadcasts and other activities we hope to arouse the professions to a realization of what is happening. We hope to make civic clubs and similar groups realize that it will take more than luncheon singing and meaningless speeches to give their clubs a purpose in life, and we want to reach labor leaders, big and little businessmen, workers in factories, farmers and all others in all walks of life, with the story, that ONLY in the greatest of unselfish and patriotic effort, can Americans live out their destiny of freedom and world leadership."

While we are on the subject of socialized medicine, if you will refer to your September, 1947 issue of the Reader's Digest you will find an article entitled "Our Most Dangerous Lobby". This article is written by Christian T. Herter, Member of Congress from Massachusetts. Also, "Our Most Dangerous Lobby—II", by Forest A. Harness, Member of Congress from Indiana, will be found in the December, 1947 issue of the Reader's Digest.

## BOOK REVIEWS

*A Text Book of Pathology*: By E. T. Bell, M. D., 6th ed. Philadelphia, Lea & Febiger, 1947. Pp. 910. Illus. Pl. Price, \$10.00.

This sixth edition of a work that has come to be accepted as a classical textbook has been thoroughly revised and is a worthy successor of the previous edition. It is a review of general pathology. The subjects discussed are necessarily brief but are comprehensive enough to be intelligible. The style is lucid and most readable. Although intended as a student text it can be read with much profit and enjoyment by the physician. The format is good. The paper and printing are most satisfying features. The index is thorough. The references are few but authoritative.

I. L. ROBBINS, M. D.

*Philosophy and Medicine in Ancient Greece*: By W. H. S. Jones, Litt. B., F. B. A. Baltimore, Johns Hopkins Press, 1946. Pp. 100. Price, \$2.00.

This is a most interesting study and should prove

of great interest and charm to the medical historian and philosopher.

I. L. ROBBINS, M. D.

*Trichomonas Vaginalis and Trichomoniasis*: By Ray E. Trussell, M. D.; with an introduction by E. D. Plass, M. D. Springfield, Illinois, Charles C. Thomas, 1947. Pp. 277. Illus. Pl. Price, \$6.00.

This is the first comprehensive presentation of information concerning *Trichomonas vaginalis* and its relationship to vaginitis. The author is particularly well qualified to consider this subject because of his careful laboratory and experimental clinical studies on the subject.

The volume takes up in logical order the morphology of the three species of *Trichomonas* found in man, their methods of propagation and transfer from host to host, and the growth requirements of these flagellate organisms *in vivo* and *in vitro*. Dr. Trussell gives particular attention to the culti-

vation of *Trichomonas vaginalis* in a bacteria-free medium, which is his own achievement.

In Part II of the monograph attention is given to the organism and its relationship to diseases of the female and male genito-urinary organs. A clear point is made that bacteria-free *T. vaginalis*, when introduced into the vagina under aseptic conditions, will at times produce a vaginitis of moderate intensity and of a type which Dr. Trussell regards as relatively peculiar to this infection. On the other hand, experimental clinical infection may produce only a carrier condition. Part III considers treatment of *Trichomonas vaginalis*. The reviewer is impressed with the very large number of drugs which have been used in attempts to clear up the infection. Such an extensive array of chemotherapeutics and procedures indicates that none is preëminently a satisfactory therapeutic agent.

The book is well documented. Much of the material is presented in tabular form and there is an extensive bibliography as well as a satisfactory index. There are a few serious errors. One is the consistent misspelling of the word "pruritus". In the second place, when referring to the *Trichomonas* of the mouth, the author uses the specific names "*buccalis*" and "*tenax*" interchangeably, confusing the reader who does not realize that "*buccalis*" has in the recent literature been replaced by "*tenax*". Possibly the most serious criticism of the volume is the style, which tends to be verbose and repetitious. It is probable that the material could have been presented to better advantage in about one-half the space.

As is usual with Charles C. Thomas publications, the book is attractively printed and bound. Unfortunately, in the copy reviewed pages 13 through 30 are missing.

ERNEST CARROLL FAUST, M. D.

*History of Medicine*: By Cecilia C. Mettler, A. B., Ed. B., Ph. D. Edited by Fred A. Mettler, A. M., M. D., Ph. D. Philadelphia, Blakiston Co., 1947. Illus. Pl. Pp. 1215. Price, \$8.50.

An historical work can only be measured accurately by the yardstick of time. However, Dr. Cecilia Mettler's "History of Medicine" promises to be one of usefulness particularly to the medical student whose desire for historical knowledge has been accelerated in recent years by newly formed societies, courses in medical schools, and by journals devoted to cultural and scientific history.

A grant provided by the Benjamin Salzer Fund enabled the author to devote nine years of patient labor to her task which was completed only a few days before her sudden death in 1944. The final editing and proof reading was done by her husband, the eminent Dr. Fred A. Mettler, Associated Professor of Anatomy, College of Physicians and Surgeons of Columbia University, who contributed the chapter on neurology and psychiatry. Early classical studies with formal training in his-

tory and in medicine had equipped Dr. Mettler for her work as historian. In 1939 she became Assistant Professor of Medical History at the University of Georgia Medical School, one of the first full-time teachers of medical history in this country. It was there that she initiated a graded series of lectures for each of the four years of the medical curriculum, and applied her correlated method of teaching to the plan of her published history.

According to the jacket, the book is intended for the practising physician and the lay reader as well as the medical student. Because of some surprising omissions of names, which the author confesses are "biographical gaps", the book will not completely satisfy those concerned with careful research and must be used with supplementary references, many of which are given in lists of selected readings that follow each chapter. Aside from minor flaws the general organization of the book is excellent and while the reading is necessarily sketchy at times and encyclopedic in form, the work is a fine achievement and will undoubtedly serve as a handy reference and guide for those who would seek more detailed information on some particular period or personality. Especially valuable are the volume's presentations of timely material and the fund of translations from ancient documents, for as the foreword tells us Dr. Mettler has "tracked down original sources, made her own translations, and compared these with previously constructed versions" . . . choosing the latter if her own offered nothing to be gained.

VERA MOREL

#### PUBLICATIONS RECEIVED

Appleton-Century Company, New York: Text-book of General Surgery (5th edition), by Warren H. Cole, M. D., F. A. C. S. and Robert Elman, M. D., F. A. C. S.

Grune & Stratton, New York: Psychopathology and Education of the Brain-injured Child, by Alfred A. Strauss and Laura E. Lehtinen.

W. B. Saunders, Philadelphia: A Manual of Clinical Therapeutics (2nd edition), by Windsor C. Cutting, M. D.; A Manual of Pharmacology (7th edition), by Torald Sollmann, M. D.; Minor Surgery (6th edition), by Frederick Christopher, B. S., M. D., F. A. C. S.; Sexual Behavior in the Human Male, by Alfred C. Kinsey, Wardell B. Pomeroy, and Clyde E. Martin.

Charles C. Thomas, Springfield, Illinois: The Pathology of Nutritional Disease, by Richard H. Follis, Jr., M. D.; Private Enterprise of Government in Medicine, by Louis Hopewell Bauer, A. B., M. D., F. A. C. P.

Williams & Wilkins Company, Baltimore: Blood Pressure and Its Disorders Including Angina Pectoris (2nd edition), by John Plesch, M. D., Budapest, M. D. Germany, L. R. C. P. and S. Edin. and Glas.



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### THE DIAGNOSIS AND TREATMENT OF ACUTE MALIGNANT OBSTRUCTION OF THE LARGE BOWEL\*

MARSHALL L. MICHEL, M. D.†

NEW ORLEANS

Recent reports on the treatment of carcinoma of the large bowel reveal excellent results in elective resection. These studies, however, pass lightly over one phase of the disease which is a frequent cause of disaster. I refer to acute obstruction of the colon due to carcinoma. Furthermore, this serious complication is infrequently discussed in its own right and often it is glossed over with brief statements to the effect that surgical decompression is the treatment of choice.

It is my impression, from a recent study<sup>1</sup> of 55 cases of acute intestinal obstruction of the colon due to carcinoma, that there is no unanimity of opinion concerning the manner in which this condition should be handled.

The 55 cases which make up this series were collected from Charity Hospital and Touro Infirmary, in New Orleans. During the three year period ending December 31, 1945, 135 patients with carcinoma of the large bowel, exclusive of the rectum, were treated at Charity Hospital, 35 of whom

(25.9 per cent) were completely obstructed. During the six year period ending December 31, 1946, 68 patients with carcinoma of the large bowel, exclusive of the rectum, were treated at Touro Infirmary, 20 of whom (29.4) per cent were completely obstructed.

In this series, 25 different surgeons were involved, one of whom treated eight of these patients, but 10 of whom were responsible for one patient each. As a result of the distribution of material among so many surgeons, there was no such uniformity of treatment as there would be, for instance, in a series of cases reported from a clinic such as Wangenstein's<sup>2</sup>. On the other hand, the high case fatality rate (almost 33 per cent) is probably more representative of the general mortality of acute malignant obstruction of the large bowel than is the far more favorable rate reported from clinics in which all cases are managed by the same general routine.

In this series, 52 of the 55 were operated on and eight different types of operative procedures were performed. In three other cases, conservative treatment was used entirely. Such a wide difference of opinion among surgeons in the same section of the country handling a similar condition, shows a lack of unanimity of opinion concerning this condition, and for this reason I believe that a closer study of this condition is merited.

#### GENERAL CONSIDERATIONS

There are certain considerations in acute malignant obstruction of the colon which set it apart as a definite disease entity and deserve special discussion.

\*Read before the Sixty-seventh Annual Meeting of the Louisiana State Medical Society, May 13, 1947.

†From the Department of Surgery, Tulane University School of Medicine and from Surgical Services of Charity Hospital and Touro Infirmary, New Orleans.

The fact that malignancy is the cause of obstruction immediately introduces the fact that the patient is in double jeopardy, both from the malignant disease and from a complication that is exceedingly serious in its own right. In obstruction due to non-malignant causes, the correction of the obstruction also corrects the cause of the obstruction. In acute malignant obstruction of the colon, the obstruction must be relieved first and resection is to be performed at a later date.

Carcinoma is by far the most common cause of acute obstruction of the large bowel. There is a general agreement that approximately 90 per cent of all obstructions of the large bowel are of malignant origin and that about one-third of all patients with carcinoma of the colon will eventually develop acute complete obstruction or such a degree of chronic incomplete obstruction that surgical decompression is necessary before resection can be performed. This series which I have studied, as already intimated, includes only the acute complete obstructions. Cases of intermittent or partial obstruction, even those which were submitted to surgical decompression prior to radical surgery, have not been included.

The incidence of acute colic obstruction in other series ranges from 35 per cent to as little as 5 per cent. Some series in which the incidence of obstruction is high include cases of subacute or chronic obstruction. Series in which the incidence is unusually low are from clinics in which little emergency surgery is done.

A second consideration, in acute malignant obstruction of the colon, is that the patients are most often in the older age group. This introduces complications not met with in younger persons, particularly degenerative diseases. Age itself, however, is not regarded as a contraindication to prompt surgical intervention. That age plays some part, however, is clear from the fact that in this series the average age of the group which survived was 53.4 years, against an average age of 55.8 years for

the whole series and of 60.7 years for the group which did not survive.

The age range in this series was from 13 to 86 years; both patients at the extremes of life, incidentally, were numbered among the survivors. That 11 of the 55 patients were under 50 years of age and that two were under 30 years of age is an interesting commentary on the all too general belief that carcinoma is a disease of middle and late life. In this series, there were 25 females and 30 males. It is of interest that 24 of the 35 cases at Charity Hospital occurred in negroes, and it is also not surprising that 10 of the 12 deaths at that institution occurred in the same race.

A third important consideration is that the patient with obstruction of the colon due to malignant disease has been ill for a considerable period of time, even if, as happens occasionally, there has been no previous evidence of disease. For a variable length of time, before the patient becomes completely obstructed, the malignant growth has been slowly reducing the patient's vitality. Often, in malignancies of the right side of the colon, marked anemia is present. In this series, it was found that a large percentage of the patients had marked deficiencies in plasma proteins. Usually, the patient has been losing weight, and, as Wangenstein<sup>2</sup> has aptly expressed it, is "autocannibalistic."

Such patients are in marked contrast to those with acute small bowel obstruction, or with large bowel obstruction of non-malignant origin, who, as a general rule, are precipitated into their acute illness from a state of previous good health. When obstruction of the colon due to malignancy is not complete, the patient can be carefully prepared for operation by replacement of the carbohydrate, protein, vitamin and hemic deficiencies, as well as by chemotherapy and bowel irrigation. Such preparation is a time-consuming process, and the patient with acute obstruction has no time whatsoever for such procedures. In most of these cases, therefore, the debility caused by the primary disease is added to the infirmities of age and the seriousness



of the acute obstruction, and the surgical risk is thereby compounded.

#### PHYSIOLOGY AND PATHOLOGY

Acute obstruction of the colon differs from acute obstruction of the small bowel in that the former is most often of the closed loop type, the growth forming the distal occlusion and the ileocecal valve the proximal occlusion. When once this loop is closed, distention of the colon is rapid, because each peristaltic wave forces the contents of the ileum into the cecum. The competency of the ileocecal valve prevents regurgitation from the cecum into the ileum. As distention increases, edema, thrombosis, ulceration and infection occur in the bowel wall until eventually, if surgical relief is not achieved, perforation will occur.

In this particular series of cases, the statement often made that perforation usually occurs in the cecum, because of its relatively thin wall and distensibility, is not necessarily true. Perforation can occur at any point above the lesion. Of the eight proved perforations in these 55 cases, only two developed in the cecum. Four of the remaining perforations were in the sigmoid, in two instances as the result of traumatic manipulation at operation. One perforation occurred in the descending colon, and one occurred at the hepatic flexure.

Wangensteen<sup>5</sup> and his associates have made important contributions, both experimentally and clinically, to the knowledge of the role of the ileocecal valve in obstruction of the large intestine. Its competency is variable. By correlation of roentgenologic observations and findings at operation, Dennis<sup>3</sup> determined that this valve was competent in 61 percent of 53 cases of acute colic obstruction. However, it is to be emphasized that attempts to differentiate clinically between a competent and an incompetent ileocecal valve are likely to delay surgical relief of the obstruction and may greatly jeopardize the patient's chances of recovery.

In every case in this series, the malignant growth was an adenocarcinoma, and in the great majority of cases it was of the

annular type, which readily gives rise to obstruction because it constricts the lumen of the bowel. In the few cases in which the growths showed gross fungating or polypoid characteristics, they also showed a marked tendency to infiltrate the wall of the colon and encircle the lumen, thus giving rise to obstruction.

#### LOCATION OF OBSTRUCTION

The exact location of an acute obstruction of the colon is an extremely important consideration from the standpoint of diagnosis and subsequent therapy. In this series, 31 of the 45 cases of obstruction occurred in the left colon. The same predominance of left sided obstruction is noted in all other reported series and can readily be explained.

The lumen of the left colon is generally smaller than the lumen of the right colon. Its walls are thicker and less distensible than the walls of the right colon. The fecal contents, which are more solid on the left than on the right, easily traumatize the malignant growth, causing secondary infection with ulceration, edema and swelling. Finally, the annular type of adenocarcinoma, which by its very nature readily gives rise to obstruction, is somewhat more frequent on the left side than on the right.

The fact, however, that 14 cases of acute malignant obstruction did occur on the right side of the colon is important to note. This contradicts a rather widespread belief that such a condition rarely occurs.

#### CLINICAL PICTURE

In cases of acute malignant obstruction of the colon, the history can often be divided into two distinct periods, one of long term, indefinite symptoms and the other of acute symptoms. However, very often the period of indefinite symptoms will be entirely absent or may blend gradually into the symptoms of acute complete obstruction.

In the typical case, the original period was characterized by an insidious onset and a triad of symptoms including: (1) altered bowel function; (2) melena, and (3) abdominal pain, which, until the onset of acute symptoms, was mild and transient.

Some patients had had previous mild acute attacks suggestive of incomplete obstruction. In a small number of cases, the development of the acute obstruction seemed to be the first manifestation of the disease.

The signs and symptoms of acute obstruction of the large bowel in this series were as follows:

1. An inability to defecate or to expel flatus. In many cases, the patients complained of a great desire to defecate. This probably explains why so many resorted to purgation before consulting a physician.

2. Cramping abdominal pain was present in practically every case. It was spasmodic and often extremely severe. Visible peristalsis was frequently present.

3. Thirty-nine of the 55 patients vomited during the acute attacks and four others complained of nausea but did not vomit. The remaining 12 patients did not complain of either nausea or vomiting. Wangenstein has commented repeatedly on the possibility that acute obstruction of the large bowel can occur without vomiting. This, in his opinion, is due to the closed loop character of the obstruction and the absence of distention or the presence of only minimal distention of the small intestine.

4. Abdominal distention was usually pronounced in acute malignant obstruction of the colon, except in cases in which a closed loop type of obstruction was present due to a colic neoplasm.

5. Abdominal tenderness was a frequent finding and was often localized in the lower right quadrant. This localization of tenderness is explained by the presence in that area of a distended cecum, which sometimes could be palpated as a tender mass, even when the malignancy was located in the left colon. Wangenstein has pointed out that this is the result of the thinness of the wall of the cecum and its greater distensibility as compared to the rest of the colon.

6. The presence of an intra-abdominal mass, which is the malignant tumor itself. Palpable growths were more often found in malignancies of the right colon, but oc-

asionally the growths on the left side could be palpated.

7. A low grade fever, which was present in a large number of cases, was probably the result of ulceration and infection of the wall of the colon proximal to the neoplasm.

The pronounced chemical changes which ensue so rapidly in obstruction of the small intestine are not present in obstruction of the colon. In this series, the only consistent abnormal laboratory findings were a slight leukocytosis, increased polymorphonuclear leukocytes, varying degrees of anemia (especially in carcinoma of the right colon), and a persistent reduction in serum protein levels.

#### DIAGNOSIS

In the majority of cases in this series the diagnosis was correct, or obstruction of the large intestine due to malignancy was listed as an alternative diagnosis. Small bowel obstruction was the only diagnosis or alternative diagnosis in six cases, volvulus in four, acute appendicitis in three, acute cholecystitis in two, diverticulitis or paralytic ileus in one case each.

An analysis of the cases incorrectly diagnosed as small bowel obstruction is instructive. In two patients the obstruction was due to carcinoma of the cecum. It is actually impossible to differentiate obstruction of the ileocecal junction due to this cause from any other type of low ileal obstruction by either clinical or roentgenological methods. Such a diagnostic error can be important, however, because some surgeons may be tempted to treat lower small bowel obstruction by intubation methods, which, as will be shown later, are definitely contraindicated in malignant obstruction of the colon. In the other cases in which an incorrect diagnosis of small bowel obstruction was made, the error was due entirely to a failure correctly to interpret the flat films or a failure to take any x-rays whatsoever.

The frequency of localization of symptoms and signs in the right lower quadrant, which has already been commented on, is the obvious explanation of the diagnosis of acute appendicitis in malignant obstruction of the large bowel. This mistake is most



likely to occur when the obstruction is on the right side of the colon, though it can also occur when left-sided lesions are present. The latter is explained by the marked distensibility of the cecum.

A low-grade fever, leukocytosis, an increase in the polymorphonuclear leukocytes, which all may be present in malignant obstruction of the colon, are further reasons for a possible incorrect diagnosis of acute appendicitis. In this connection, the following case is of special interest.

A 32 year old woman had had recurrent attacks of pain in the right lower quadrant, nausea and vomiting for six months. A few days after the latest attack, she was operated on through a right rectus incision, with a diagnosis of acute appendicitis, which was not verified by the surgeon at operation or by the pathologist. She returned to the hospital two weeks after her discharge, with the same symptoms as before operation and with marked abdominal distention. A barium enema at this time permitted a diagnosis of obstruction due to carcinoma of the sigmoid colon, which was relieved by colostomy.

Carcinoma of the colon introduces a reverse diagnostic problem in acute appendicitis. In Boyce's<sup>6</sup> material on acute appendicitis, collected over an almost 16 year period from Charity Hospital, three patients over 40 years of age died without operation from appendiceal peritonitis because the diagnosis of carcinoma of the colon had been made. In six other cases, operation was delayed because of a similar mistake in diagnosis. One of these cases ended fatally, because the patient was being prepared for surgery with the idea of a colectomy being performed.

It is of interest that in some of the cases in which the right side of the colon was resected for obstructing malignancy, the pathologist reported the appendix to be acutely inflamed. These pathologic changes are the result of back pressure, which causes inflammatory changes in the wall of the appendix, just as in the wall of the

cecum and the colon proximal to the obstructing growth.

The incorrect diagnoses are significant from the standpoint of their responsibility for a delay in surgical therapy. A patient with obstruction due to a paralytic ileus is not likely to be operated on at all. A patient with cholecystitis may or may not be operated on. Many surgeons may not operate immediately for presumed simple obstruction of the lower ileum.

On the other hand, a patient with volvulus and a patient with acute appendicitis is usually operated on without delay and these particular errors, fortunately, were in the category of conditions which demand prompt operation. However, it is to be emphasized that in dealing with acute malignant obstruction of the colon the importance of an exact diagnosis beforehand cannot be too strongly emphasized. Abdominal exploration in such cases definitely places the patient in a more precarious situation.

In this series, the fact was brought out that the majority of patients had had abdominal symptoms for relatively long periods of time before seeking medical advice. It is true that unless an individual seeks medical aid, medical aid cannot be given to him. The importance of early diagnosis in cancer and the value of our present campaigns for increasing the layman's knowledge of the disease is well brought out.

However, on the other hand, it is ironic and tragic that eight patients in this series did seek medical aid, at intervals varying from one to eight months before they entered the hospital with acute malignant obstruction. The patients all consulted their physicians because of abdominal symptoms, particularly vague abdominal pain. Three patients were told by their physicians to take purgatives. One was treated for seven months for dysentery, which he might or might not have had also. The presence of dysentery bacilli or ameba in the stools does not rule out the presence of a concurrent neoplasm. One patient was told that he had a gastric ulcer and another was told that her abdominal symptoms were due

to a gynecological disturbance. The conclusion is inevitable that in none of these cases was the slightest attempt made to study the patient exhaustively and to arrive at an accurate diagnosis, though most of them presented the well-known triad of altered bowel function, melena and cramping abdominal pain.

#### ROENTGENOLOGIC DIAGNOSIS

X-ray studies of the abdomen, both by flat plate and barium enema, are of extreme importance in making a correct diagnosis in acute malignant obstruction of the colon.

In this series, flat plates were made in practically all cases with generally uniform findings, in the form of marked distention of the colon up to the site of growth. Distention of the small intestine was present in a larger proportion of cases than the writings of Wangenstein might indicate.

The presence of distention of the small intestine can be explained in several ways. When the ileocecal valve is incompetent, naturally the small intestine takes part in the distention. Even when the valve is competent, and a so-called closed loop obstruction is present, it is logical to assume that pressure in the cecum will eventually reach such a point that the valve cannot open in response to ileal peristalsis and small bowel distention will eventually occur.

Furthermore, when pronounced distention of the large bowel is present, plus extensive inflammatory changes in the wall of the colon, some degree of paralytic ileus is likely to take place in the small bowel. The chief importance of the presence of small bowel distention in association with large bowel obstruction is that the primary source of the occlusion may be overlooked and decompression by non-surgical methods may be substituted for surgical decompression.

It should also be noted that carcinoma of the cecum with involvement of the ileocecal valve causing obstruction presents roentgenologic findings distinctly different from those observed in occlusion elsewhere in the large bowel. In such cases there is no distention of the colon and the findings are typical of low ileal obstruction.

The plain film should be taken with the patient in the upright position. Additional information often can be gained from the upright film that is not evident from a film taken with the patient lying down.

An immediate barium enema should always be done in cases in which malignant occlusion of the colon is suspected. In the series which we have reviewed, this method of examination was used before operation in only 15 of the 55 patients. It seems significant that it was not employed in any of the incorrectly diagnosed cases. Even if the diagnosis of colonic obstruction can be definitely made without the assistance of the roentgenogram, the barium enema is necessary for exact localization of the growth, so that the incision can be correctly placed in reference to it and that exploration at operation can be reduced to a minimum. Furthermore, if the growth is accurately located before operation, the exact operative procedure can be decided upon beforehand and can be done rapidly with a minimum of manipulation.

Certain precautions, of course, are necessary. The barium must be introduced gently and slowly and under low pressure. Care must be taken that it is not forced past the site of obstruction for two reasons. In the first place, the exertion of undue pressure can readily cause perforation of a friable, secondarily infected intestinal wall, infiltrated with malignancy, which lacks the distensible properties of the normal colon. In the second place, if barium is forced past an incompletely obstructing growth, the possibility exists that the obstruction may be completed. If barium remains in the right side of the colon for even a short period, the normal absorptive properties of the colon soon reduce the barium to an inspissated mass which can completely block the intestinal lumen. A case of this kind, which is not included in this series, recently came under my observation.

Useful as barium is in the diagnosis of obstruction of the large bowel when given as an enema, it is extremely dangerous when given by mouth in any type of intes-



tinal obstruction. An incomplete obstruction may be converted into a complete one, the presence of the opaque medium in the bowel can greatly complicate the operation, and the risk of perforation is greatly increased. In one case in this series, in which conservative treatment was used, a dual perforation of the bowel in the transverse colon and sigmoid, and fatal generalized peritonitis followed immediately on the use of barium by mouth as a diagnostic measure.

#### TREATMENT

That there is a lack of uniformity of opinion concerning the handling of acute malignant obstruction of the colon is evident from this series which I have reviewed. Three of the patients were treated conservatively, and eight different types of operative procedures were performed in the other patients.

There is no question but that prompt surgical decompression of the colon is indicated in acute malignant obstruction of the colon regardless of the exact site of the lesion. This opinion is also that of Wangenstein,<sup>5</sup> Dennis,<sup>3</sup> Rankin,<sup>4</sup> and others. Conservative therapy and attempts at intestinal intubation have no place whatsoever in the treatment of acute malignant obstruction of the colon.

*Conservative therapy:* In three patients in this series, conservative treatment was used completely. Two of these cases terminated fatally in the hospital. Necropsy examination in the first, a carcinoma of the sigmoid, revealed generalized peritonitis following perforation of the bowel at the hepatic flexure. In the second, a carcinoma at the hepatic flexure, the patient died suddenly after 15 days of hospitalization, with signs and symptoms suggestive of perforation of the cecum. The fact that one of these three patients was able to overcome the obstruction after conservative treatment is certainly no indication that this is the correct way to handle such cases. The physician who elects to treat complete malignant obstruction of the large intestine by conservative measures is indulging in wishful thinking. As Pfeiffer and Martin<sup>7</sup> have

put it, "relief by this means may be hoped for but should not be expected."

In patients in whom the obstruction of the colon due to carcinoma is not complete, close observation must be the policy. If there is any question of the obstruction becoming complete, surgical decompression should be undertaken as soon as possible because of the possibility of closed loop obstruction and perforation of the colon.

Due to the fact that the onset of complete obstruction is occasionally insidious, it is evident that surgical decompression is often unnecessarily delayed while the patient is in the hospital. In seven of the 15 patients who died, operation was delayed from two to 14 days. In eight of the 37 patients who survived operation, surgical intervention was delayed from 10 to 34 days. The obstruction was temporarily relieved and the patient treated from 10 and for 34 days, respectively, but in each instance it recurred as soon as treatment was discontinued and surgical decompression had to be resorted to.

In at least three cases in this series, there seems little doubt that while an incomplete obstruction was being treated conservatively, the obstruction became complete. In another case, the patient was being prepared for elective colectomy for carcinoma of the cecum by the use of castor oil. In the course of the preparation, she developed signs and symptoms of acute obstruction, for which ileostomy was performed. Death occurred 48 hours later, and necropsy revealed an obstructing carcinoma of the cecum which had perforated.

That intestinal intubation with the Miller-Abbott tube is of permanent, curative value in any type of obstruction of the colon is not now generally believed. In this series, it was practiced in 20 cases, but the tube entered the small intestine in only three cases, two of which terminated fatally. Although it is entirely permissible to use the tube in conjunction with surgical decompression, the use of intestinal intubation is certainly not a substitute for surgical decompression in such cases. When the ileocecal valve is competent, the colon is

unable to empty its contents in the direction of the ileum, although the ileum itself is able to evacuate itself into the cecum, with a resulting increase in a distention which is already present. The length of time necessary for a Miller-Abbott tube to traverse the distance from the stomach to the ileocecal junction is entirely too long to delay decompression of the large bowel proximal to the growth.

The tube is useful only when it can be passed with a reasonable degree of speed (which can be increased by the use of mercury in the balloon, as suggested by Harris<sup>8</sup>) and thereby can deflate edematous, distended loops of small intestine which may be present and prevent further influx of the contents of the small intestine into the cecum. It usually has no other influence on a large bowel distention and such relief if secured may be highly misleading, thus leading to further delay.

These remarks, of course, have nothing to do with the use of intubation after operation, which should be routine in all surgery of the large bowel. Simple duodenal suction is usually all that is necessary, but the Miller-Abbott tube should be employed if small bowel distention is pronounced. One criticism which can be advanced against the postoperative treatment applied in this series was that in many cases the impression seems to have occurred that because the Miller-Abbott tube was not effective before operation, it would also be of no value after operation and was therefore removed.

#### RESECTION IN THE FACE OF OBSTRUCTION

In this series, immediate resection was carried out 10 times, with a mortality of 50 per cent. Five resections were done for carcinoma of the sigmoid, with two deaths; two in obstruction of the cecum, with two deaths; and once each in carcinoma of the hepatic and splenic flexures and of the right transverse colon. The patient with carcinoma of the splenic flexure also died.

This is a prohibitive mortality, and the performance of resection in the face of acute obstruction of the colon reveals a fundamental misconception of the patho-

logic background of the disease. As already intimated, there are two distinct problems to be dealt with. One, which is urgent and immediate, is the relief of the obstruction before the viability of the intestinal wall is irreversibly damaged by impairment of circulation. The second problem, which is not immediately urgent, is the removal of the malignant tumor. This should be dealt with at subsequent operation after the obstruction has been overcome.

When resection is done in the face of obstruction, all circumstances are against success. The condition of the patient is frequently very poor. The blood supply to the intestinal wall is impaired. The mucosa is ulcerated and infection of the bowel wall is present. The patient is dehydrated, starved and exhausted, and he may show impairment of the vascular system.

Immediate resection is certainly a temptation which always has to be faced when operating on such cases. It seems highly significant that the only patient in the group of fatal cases who was considered to be a good risk before operation lost that advantage when immediate resection was attempted in the face of obstruction. Two patients in the group of survivors who presented fair risks when they were first seen also lost that advantage when immediate resection was attempted. The pathologist reported that in these two instances the growth had been incompletely removed.

Resection was done as a subsequent operation in 22 of 32 patients who had surgical decompression only at the first operation. Of these 22 patients, there was only one fatality, which was the result of massive atelectasis. Had resection been attempted in these cases at the first operation, it seems fair to assume, on the basis of five deaths in the 10 cases in which resection was done in the face of obstruction, that a similarly prohibitive mortality would have occurred.

#### SURGICAL DECOMPRESSION

The type of surgical decompression which should be used depends on the location of the obstruction. For this reason, definite localization of the growth by means



of the barium enema before operation is indicated.

In acute malignant obstruction of the left colon (left half of the transverse colon, descending and sigmoid colon), the choice of operation lies between cecostomy and transverse colostomy.

Cecostomy was done in 24 patients in this series, with six fatalities. That cecostomy is frequently a life-saving measure and is a simple operative procedure there is no doubt. Another advantage of cecostomy is that very often it closes spontaneously.

However, there are numerous disadvantages to cecostomy in acute malignant obstruction of the colon. Aseptic decompression is seldom possible. Drainage of the bowel contents frequently occurs directly onto the skin. The operation may be difficult and dangerous when the bowel wall is thin and distended. Exteriorization of an intact segment of the cecal wall is often impossible and decompression is usually accomplished at the expense of some soiling. Decompression is less effective than when colostomy is performed. Defunctionalization is not achieved. Infection of the wound is common and wound dehiscence is not infrequent. If spontaneous closure does not occur, surgical closure may be difficult.

In my opinion, the operation of choice in acute obstructing malignancy of the left colon is a simple loop colostomy of the right side of the transverse colon. In this series, it was performed in only four patients.

Such an operative procedure has numerous advantages. The intestinal opening is considerably removed from incisions used for subsequent resection of left-sided growths. The operation is easily performed, for the transverse colon is very mobile and easily delivered. If the operation is performed through a small transverse incision, extrusion of the distended bowel is practically spontaneous. This is not as easily accomplished through a vertical incision, because of the twisting of the bowel on its axis. The use of a glass or plastic rod to support the bowel eliminates the necessity for suturing the colon to the layers of the abdominal wall.

Immediate decompression is obtained by placing catheters in both loops of the colostomy for 48 hours before the bowel is actually severed.

This procedure is further simplified by the adoption of Wangenstein's<sup>5</sup> suggestion that during roentgenologic examination a small opaque object be placed over the umbilicus, for later identification of the exact location of the transverse colon. Incision can then be placed directly over the colon and manipulation reduced to a minimum.

When transverse colostomy is done, defunctionalization of the bowel is almost complete. The patient can be ambulated rapidly and can usually consume his usual diet. The material which accumulates in the distal colon can be easily evacuated by means of irrigation.

Surgical closure is necessary in such colostomies, but is not particularly difficult. End-to-end closure can readily be performed after adequate chemotherapy, and the complications and difficulties of spur formation and spur crushing are avoided.

Good results of the simple loop transverse colostomy are evident in such a report as Fallis'<sup>11</sup> which shows 52 such operations for obstruction of the left colon, with only two deaths.

Devine was the first to suggest the utilization of the right half of the transverse colon as the site of a temporary colostomy for lesions of the left colon. A special type of procedure was prescribed and such colostomies were done in three patients in this series. Defunctionalization is complete and satisfactory by this method, but in my opinion this procedure is unduly complicated and has no advantages over a simple loop colostomy in acute left colic obstruction.

In this series, three colostomies of the sigmoid colon were done directly above the site of the growth. Such a procedure is not desirable because of the resulting fixation of the left side of the colon and technical difficulties involved in subsequent resection. There is a uniformity of opinion, among those who have studied this condi-

tion, that some type of right-sided decompression (either cecostomy or colostomy) should be done in left-sided obstruction and that no manipulation or exploration of the lesion is indicated.

Right-sided malignant obstruction of the large bowel presents a different problem from that of obstruction of the left colon. The choice of operative procedure for right-sided malignant obstruction lies between cecostomy, ileostomy, or ileotransverse colostomy. Cecostomy, as has previously been mentioned, is an adequate procedure for decompression of the colon and is particularly useful in obstructing carcinomas which occur either in the ascending colon, hepatic flexure, or right side of the transverse colon. Naturally, it is of no use and should not be performed in obstructing carcinoma of the cecum or ileocecal region. One disadvantage of cecostomy is that the right side of the colon is fixed to the abdominal wall and subsequent resection may be rendered somewhat difficult.

As Rankin<sup>4</sup> suggested some 20 years ago, and as Wangenstein<sup>5</sup> also advocates, it is a feasible plan in obstructing carcinoma of the right colon to open the terminal ileum and insert the catheter through the ileocecal valve into the cecum and perform a catheter ileostomy. Such a procedure would perform essentially the same degree of decompression as a cecostomy or appendicostomy. Ileostomy was performed in only two patients in this series, and both died. However, both patients were moribund when operated upon, and the value of the procedure cannot be judged from these two isolated cases.

In right-sided obstruction, ileotransverse colostomy, producing a short circuit around the growth, has certain advantages over enterostomy. At subsequent operation there is no enterostomy to be dealt with and there is no fixation of the right side of the colon. It is undoubtedly a safe and useful procedure in selected cases, in which the intestine proximal to the growth is not markedly distended and in which the ileocecal valve seems to be incompetent. However, it is more time-con-

suming than a simple enterostomy. This is a serious consideration in gravely ill patients.

On the other hand, if the ileocecal valve is competent, the closed loop may still persist after the performance of ileotransverse colostomy. Therefore, some type of decompression may be necessary in addition to the ileotransverse colostomy. An excellent procedure is to completely sever the ileum and bring the distal end out as a mucous fistula.

In the six persons in which ileo-transverse colostomy was done, an ileostomy was utilized as an adjunct in one case, while in another case the surgeon performed appendectomy, decompressed the cecum via the appendiceal stump and then closed the stump.

#### OTHER THERAPEUTIC CONSIDERATION

*Anesthesia:* My personal preference, in such cases in which abdominal distention is marked, is for the use of spinal anesthesia. The maximum of relaxation is obtained, and excessive respiratory movements, which are likely to be present during general anesthesia, are not encountered. If the patient is unduly apprehensive, nitrous oxide, ethylene or sodium pentothal can be added.

The frequency with which patients come to the operating table with gastric, duodenal or Miller-Abbott tubes in situ may complicate the use of general anesthesia, but the latter is perfectly feasible if spinal anesthesia is contra-indicated and if a competent anesthetist is available.

In this particular series, competent physician-anesthetists were available in all cases, and in no instance did the anesthesia *per se* play any part in the fatal outcome.

*Chemotherapy:* Chemotherapeutic and antibiotic agents were used in only 15 of the 55 cases in this series. This number included five of the 18 fatal cases. Whether a wider use of these new agents would have reduced the number of fatalities, it is impossible to say. However, it is my opinion that the unwise surgical procedures which were used in some of the cases and long periods of temporizing measures introduced



in others were really the important factors in the mortality and that the addition of chemotherapy would have had little effect.

My own opinion is that sound surgery is of preeminent importance in the condition herein discussed, but the adjunct use of penicillin in massive doses postoperatively is justified. The method recently described by Crile<sup>12</sup> for appendiceal peritonitis, in which doses of 100,000 units of penicillin every two hours are given intramuscularly, can readily be applied in acute malignant obstruction of the colon in which perforation may occur.

*Suture material:* In this particular series, the four incidents of wound dehiscence are perhaps the proportion to be expected in a series of cases of malignant obstruction due to carcinoma of the colon. No particular conclusions can be drawn as to why these occurred, because of the numerous varieties of suture material which were employed by the 25 surgeons involved. The level of protein deficiencies in these patients was, of course, important.

My personal preference is for the use of fine cotton for the closure of abdominal wounds, particularly in such cases as these. I also believe that the incidence of wound infection can be markedly reduced by the use of secondary wound closure in all cases in which contamination has occurred.

#### MORTALITY

Three previous series of cases of intestinal obstruction studied at New Orleans Charity Hospital invite comparison with this series. In the first, reported by the late C. Jeff Miller<sup>13</sup> in 1929, there were nine cases of malignant obstruction of the large bowel, with seven deaths. In the second, reported by Moss<sup>14</sup> in 1934, there were four instances of this type of obstruction, with two deaths. In the third, reported by Boyce<sup>15</sup> in 1937, there were 11 such cases with nine deaths. Case fatality rates for these early series are higher than those for the series which I have reported (32.7 per cent), but this latest series also bears out Rankin's gloomy prophecy that "even with the simplest possible surgery the case fatality rate for this type of obstruction

will be at least 30 per cent, and the rate will rise proportionately as more extensive surgery is done."

#### CAUSE OF MORTALITY

It is evident from a study of this series, that the high mortality rate can be attributed to the following: (1) attempts at conservative therapy; (2) resection in the face of acute obstruction; (3) delay of patients seeking medical attention; (4) delay in diagnosis after the patient is seen by a physician; (5) attempts at surgical exploration at operation with resulting perforation of the growth due to trauma; (6) the use of purgatives; (7) the use of barium by mouth; (8) the patient's age; (9) associated systematic disease; (10) debilitation due to metastasis.

#### SUMMARY

1. Fifty-five cases of acute obstruction of the colon due to carcinoma have been analyzed.

2. A lack of uniformity of treatment and a mortality of 33 per cent indicate a necessity for further study of this condition.

3. The patient is in double jeopardy from the obstruction and from the carcinoma. The obstruction must be treated first.

4. The age and the duration of the malignant disease add to the risk.

5. Obstruction of the colon is most often of the closed loop type.

6. In 31 cases the obstruction was in the left colon.

7. The clinical picture presents two phases: (1) longstanding signs and symptoms; (2) acute complete obstruction.

8. An exact preoperative diagnosis of the site of obstruction is important and can be readily determined by the flat x-ray plate of the abdomen and the barium enema.

9. Conservative treatment and resection (in the face of obstruction) cause a prohibitive mortality.

10. Simple loop colostomy of the right side of the transverse colon is the treatment of choice in obstructing carcinoma of the left colon.

11. Cecostomy, ileostomy, or ileotransverse colostomy are the procedures of

choice when the obstruction occurs in the right colon.

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## EPIDEMIOLOGY AND RECENT DEVELOPMENTS IN POLIOMYELITIS\*

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## INTRODUCTION

Poliomyelitis as a disease has attracted the attention of lay individuals, laboratory workers and members of the medical profession for well over a century and a half.

The recognition of the existence of the disease is noted by many as dating back to 1600 B.C. Actually the first good clinical description of the disease is made by Underwood in a paper entitled "Debility of the Lower Extremities" published by J. Mat-

thews in London, England in 1789.

In recent years a great deal of interest has been manifested in this disease and but few diseases can boast as much interest as has been centered around poliomyelitis. This interest has centered around the mode of transmission of the disease, prevention and treatment. A great deal of progress has been made along these particular fields, but the sum total of our knowledge of the disease is still rather limited—limited at least from the point of view of practical application.

## ETIOLOGY

Although there are proponents of the bacterial etiology of the disease, it is generally recognized that the causative agent is a virus. There is also general agreement that the poliomyelitis virus is a neurotropic virus which probably is disseminated through the body by passage along the nerve fibers. More specifically, Toomey<sup>1, 2</sup> believes that the virus travels best along non-medullated or gray nerve fibers.

In 1909 Flexner and Lewis<sup>3</sup> described a virus as the etiologic agent of this disease and described in detail their experimental work with the M. Rhesus monkey. By cerebral inoculation of macerated spinal cord tissue, experimental animals developed a disease closely simulating infantile paralysis. The isolation of this virus and experimental work herein described have been repeated many times since.

## THE PORTAL OF ENTRY

Although it is generally agreed that the virus of poliomyelitis is a neurotropic virus which enters the central nervous system by traveling along nerve tracts there has been no agreement as to ways and means by which this virus reaches the nerve tracts. There are two concepts which may be mentioned as to the portal of entry of the virus, namely the nasopharynx and the intestinal tract.

Toomey<sup>1, 2</sup> is the principal proponent of the gastrointestinal route of entry. By experimental inoculation of the virus into the gastrointestinal tract, Toomey was able to produce a disease in monkeys which simulated poliomyelitis. However, he was obliged to create severe stagnation of the gastro-

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intestinal tract before he could promote the development of this condition in his experimental animals. Other investigators are of the opinion that such unusual stagnation is probably non-existent normally and therefore the gastrointestinal work of Toomey and his associates should be looked upon as additional good scientific information without a great deal of practical application value.

Sabin and his associates<sup>4</sup> are proponents of the olfactory route of entry. This theory probably has more supporters than any other theory. Proponents of the theory point out that the virus has been isolated from the nasopharynx of cases and apparently healthy carriers; further that the epidemiologic characteristics of the disease suggest a droplet type of infection. Supporters of this theory also point out the ease with which entrance into the olfactory system might be brought about through the nasopharynx. Certainly the virus has been isolated in acute cases from the nasopharynx. All of these facts taken together are strongly suggestive of the nasopharyngeal route of entry of the virus.

#### ESCAPE

The escape and liberation of the virus from the human body have been repeatedly studied and innumerable publications are available for study.<sup>5</sup> The virus of poliomyelitis has been isolated from the stools and nasopharynx of apparently healthy carriers and persons acutely ill with the disease. The virus in the nasopharynx is usually present only for relatively short periods of time. The virus, however, may be present in the gastrointestinal tract weeks before the onset of clinical symptoms<sup>6</sup> and for months after the acute symptoms have subsided. There is of course a question which arises in the minds of investigators as to whether or not the primary localization of the virus is in the upper respiratory tract and that the gastrointestinal localization is secondary and is brought about by the swallowing of sputum contaminated with the virus.

#### RESERVOIRS

Although extensive research work has

been directed at the recognition of reservoirs of this virus, there is but one definite reservoir known, namely, that of the human being. The reported recovery of the virus of poliomyelitis from a mouse found dead in a home where there had been a case of poliomyelitis only adds greater confusion to an already confused situation. To the best of the speaker's knowledge, this finding has not been repeated. Fowls, birds, rodents and various other animals have been examined but without satisfactory recognition of the poliomyelitis virus.

The virus has been isolated from sewage<sup>7</sup> and it has been shown that it will resist<sup>8</sup> the effect of chlorine in concentrations of 0.5 per 1,000,000 parts for over a half hour. There have been variously reported outbreaks which according to the epidemiological evidence would tend to incriminate food and milk, but all of these factors are affected by missing links of information and certainly it has been repeatedly pointed out that the pattern of behavior of poliomyelitis is such that it does not correspond with the characteristic behavior of food or water-borne infections.

The recognition of the virus in the nasopharyngeal secretions of persons affected with the disease and the recognition of the virus in sewage<sup>7, 9, 10</sup> and its presence in the stools of apparently healthy persons<sup>5</sup> lends emphasis to the significance of the human reservoir. The repeated recognition of the virus in apparently healthy human carriers and the rapid development of the carrier state is reported by Brown, Francis and Peerson: Certainly the report of the recognition of the virus of poliomyelitis nineteen days before the development of clinical symptoms in the stool of an apparently healthy individual<sup>6</sup> is a notable contribution to the knowledge of poliomyelitis.

#### MODE OF TRANSMISSION

There is no definite agreement as to the mode of transmission of this disease. The virus of poliomyelitis has been isolated from the nasopharyngeal washings of apparently healthy individuals as well as those suffering from the disease. It has been isolated from sewage, from food and

from the gastrointestinal tract of flies. This wealth of confusing facts only lends further confusion to the possible ways and means by which this disease is transmitted. It has also been proposed only because of some epidemiologic evidence that possibly the disease is transmitted by insect vectors.

Certainly the epidemiologic characteristics of the disease are such that they do not coincide with water or food-borne diseases. Water and food-borne epidemics are usually explosive in nature and affect large numbers of people simultaneously. Usually epidemics of poliomyelitis are progressive, develop gradually, show evidence of radial spread and reach their peaks within several weeks from the date of onset. The distribution of cases within the area affected is scattered with occasional aggregation, while in water-borne epidemics the distribution is somewhat more uniform. The attack of poliomyelitis in urban epidemics seldom exceeds one per one thousand and in rural epidemics the attack rates seldom exceed three per thousand. In food and water-borne outbreaks the attack rate among exposed persons is usually much higher.

One cannot too emphatically discount the food and water bases as the modes of transmission because as has been noted many times the rate of infection with poliomyelitis virus probably far exceeds the incidence of reported cases. Proponents of the food and water-borne mode of transmission therefore have this very important argument in their favor.

Probably the oldest and the best theory of the mode of transmission of poliomyelitis is that of person to person contact and droplet infection. Certainly the number of persons succumbing to the disease who have had contact with other cases is statistically significant. An investigation which has been carried on evidence of contact with cases has been reported as high as 60 to 80 per cent. There are contradictory points to this method of transmission. The low secondary attack rate, intra and extra-familially, is certainly suggestive of some important extrinsic or intrinsic factors limiting the occurrence of secondary cases. There is also

the important fact that additional cases in families and households may develop in subsequent years in persons who escaped the first exposure.

#### AGE, SEX AND RACE DISTRIBUTION

The disease affects primarily persons between the ages of five and fourteen years of age with a reasonably high incidence under four and with greatest concentration of cases between five and nine years. The disease, however, does affect persons of all ages and the speaker has had the experience of seeing a case seventy years of age and has seen poliomyelitis in a new-born infant.

By sex, the distribution of the disease shows a somewhat greater incidence among males than among females, the ratio being approximately 1.4 males to one female. A great deal has been said and written about the racial distribution of poliomyelitis depending almost entirely upon the section of the community or section of the country which is affected. My associates and I have not been able to show any difference in the race distribution of poliomyelitis. By individual epidemics difference of significant amount has not been noted, but over a period of many years the attack rate among negroes and whites is approximately the same. The differences which have been noted in attack rate by race were due to geographic or area location of the epidemic.

The rural as against the urban incidence of the disease is noteworthy. In the most severe urban outbreaks the incidence of the disease seldom exceeds one per 1,000 population while in rural areas when epidemics occur the attack rates are two or three times as great as in urban areas. As a matter of fact the actual incidence of the disease—the rural against urban—shows a much greater incidence in the rural areas than in the urban. The rural incidence of poliomyelitis is so much greater that it is frequently referred to as primarily a rural disease. The Henderson County outbreak of 1945 in Tennessee is a good illustration of this theory.

There is a definite seasonal variation of the disease. It has been repeatedly noted



that poliomyelitis has an apparent selective occurrence both as to season and individuals. Epidemics seem to occur in summer and early fall and as previously noted, clinical poliomyelitis affects but a very few persons who live in the epidemic area.

#### SEASONAL VARIATION

The seasonal variation is of significant epidemiologic importance because coupled with this seasonal variation is the fact that the incidence of paralytic disease in areas where seasonal changes are not so radical is considerably lower than in the more temperate climates where the seasons change and change radically. This has brought about the prognostication that possibly there is something in the physiology of the human being which in part at least is related to the possibility of successful and clinical invasion of the virus. In other words, the prognostication is that a certain percentage of the people in these areas fail to make adequate physiologic adjustments with the varying climate and season with the end result that the infection with poliomyelitis virus results in clinical disease. On the other hand, the person whose physiology follows a more favorable pattern of adjustment is infected but escapes clinical disease.

#### PREDISPOSING FACTORS

There is a great deal of evidence to suggest that there is a hereditary predisposition to poliomyelitis and that the clinical disease is prone to recur in families. This fact is proposed along with drawing attention to the fact that the incidence of secondary cases in households during the same epidemic is rather infrequent. In a survey of the incidence of poliomyelitis in families, Aycock pointed out that 51 per cent of the cases gave a history of disease among relatives while only five per cent of his controls gave a similar history.<sup>11, 12</sup>

Further investigations by other workers, notably Adair and his associates<sup>13</sup> confirm his familiar predisposition to poliomyelitis. There have been attempts by Aycock and Draper to associate the disease with endocrine imbalance and to point out that certain institutional types<sup>14</sup> are more apt to acquire clinical poliomyelitis than are oth-

ers. Aycock further suggests that susceptibility may reside in a subclinical endocrine difference and more particularly a subclinical difference between periods of growth and development. These theories needless to say cannot be completely ignored but evidence to the contrary is proposed by other investigators.

Aycock also points out that there appears to be a predisposition to attacks of poliomyelitis among pregnant women. He noted that poliomyelitis is associated with pregnancy about four times as frequently as it would be expected in non-pregnant individuals. The closer examination of this relationship shows that the greatest risk occurs in the second and third trimester of pregnancy.<sup>15</sup>

Here again Aycock draws attention to the fact that this may be associated with some endocrine disturbance. Experiments have been attempted by Jungblut to associate the incidence of the disease with vitamin C deficiency. Helm<sup>16</sup> has proposed that vitamin B is the major factor for increased susceptibility for the virus and Weaver in turn<sup>17</sup> in his experimentation with cotton rats was unable to show any relationship between vitamin B deficiency and the poliomyelitis virus.

It is conceivable therefore that the endocrine and vitamins, or the lack of endocrines or vitamins, is associated with susceptibility to clinical poliomyelitis. If there is an intimate association the method of its operation is not clearly understood.

Certainly from the overwhelming amount of information which is available, it is obvious that the incidence of infection with poliomyelitis virus far exceeds the reported incidence of clinical disease.

It has also been noted by some investigators that trauma, over-exertion and exhaustion are predisposing to clinical poliomyelitis. One must question this proposition because although trauma may be very definite, the degree of trauma may be variable or at least the interpretation placed upon the severity of such trauma by the investigator is variable. Also, exhaustion and over-exertion are relative terms. In the Detroit

studies virtually no correlation existed between these factors and the incidence of the disease. The incidence of severe poliomyelitis among recently tonsillectomized persons is quite significant. For example, there is evidence to indicate that recently tonsillectomized children develop bulbar poliomyelitis much more frequently than those children who have not recently been tonsillectomized.<sup>18</sup> There are, of course, persons who do not agree with this. But the evidence is overwhelmingly in favor of the proponents of the predisposing effect of tonsillectomies to the development of bulbar poliomyelitis.<sup>19</sup>

#### CARRIERS

As has been previously noted the incidence of infection with poliomyelitis virus far exceeds the incidence of clinical cases.<sup>5, 6</sup> My associates and I were able to show that in one outbreak involving an institution caring for children between infancy and ten years of age, several individuals without any clinical symptoms were found to be carriers of the virus of poliomyelitis. A nurse and a physician, in addition to several of the children, who had intimate contact with cases were found to be positive. It seems quite possible that abortive and sub-clinical cases may carry the virus for varying periods of time. Brown and his associates, for example, were able to show that a person who developed clinical poliomyelitis had actually harbored the virus of poliomyelitis in his stools nineteen days before the onset of the first clinical symptoms.

#### PREVENTION

The principals of prevention of poliomyelitis have varied many times even within the past decade. Vaccines have been developed which have been most unsuccessful. Prophylactic spraying of the nasopharynx with various and sundry chemicals has proved to be a total failure. As a matter of fact there are observers who believe that both the vaccine and the nasal spraying had actually the opposite effect of that which was expected.

The closing of schools, the avoidance of crowds and the isolation of the patient and contacts appear to have the effect of only

a placebo. Certainly the wide and general distribution of the virus in nature and among humans particularly precludes the possibility of any effective means of avoiding possible infection. Based upon these facts the rules and regulations for the control of communicable diseases have brought about a change in attitude towards the isolation of poliomyelitis cases and contacts. Presently but few states isolate cases and contacts.

#### SUMMARY

The only significant statement which a person can make as far as prophylaxis of poliomyelitis is concerned is that up to this time nothing has been found to be effective and the only encouraging statement which can be made is that clinical and research efforts are ever expanding in the hope of finding some effective ways and means through which preventive measures may be exercised.

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## DICOUMARIN—MEDICAL ASPECTS\*

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NEW ORLEANS

To the great discredit of the internist, thrombo-embolism is today widely regarded as a surgical problem. Actually, of course, it is a phenomenon apt to arise whenever bed rest and immobilization for even a few days are imposed upon the patient for any reason, but the medical profession is indebted chiefly to the surgeon for the current interest in this insidious threat to life. There is as yet no unanimity of opinion as to the optimum methods of prevention and treatment but new weapons are available and new records are being set. This paper will be concerned with the application of one of the newer anticoagulants, dicoumarin, 3,3'-methylenebis (4-hydroxycoumarin)], to the prevention and treatment of intravenous clotting.

### THROMBO-EMBOLISM OF PERIPHERAL ORIGIN

Those who feel that venous thrombosis is predominantly a postoperative problem should examine the careful leg dissections reported by Hunter and coworkers<sup>1</sup> which showed that intravascular clots developed in about 60 per cent of middle-aged and older individuals put to bed for even a few days, an event generally attributed to circulatory stasis and possibly also to hypercoagulability of the blood. Similar studies have, of course, been made before, and all authors are agreed on the frequency and menace of these loosely attached clots. There is considerably less agreement, however, regarding the best method of coping with venous thrombosis. The prophylac-

tic importance of ambulation or leg exercises is illustrated by the observation that the incidence of venous thrombosis in the legs of those so treated up to 48 hours before death was 18 per cent, whereas in those inactive prior to death it was 53 per cent.<sup>1</sup> The further importance of deep breathing to accelerate the return of blood to the thorax and of compression bandages around the leg to increase the rate of blood flow through the deeper veins has been repeatedly advocated by Ochsner.<sup>2</sup> No one can estimate the number of lives which have been saved by the adoption of these sensible measures, but certainly no one can maintain that they are completely effective. We have, for example, in one year seen seven deaths from pulmonary embolism on a hospital service where these measures have been routinely adopted and keenly enforced.

Because prophylaxis against clotting frequently fails, venous ligation is now widely advocated as a method of protecting the patient from detachment of the clot. Bilateral ligation of the femoral veins is said to be a safe and adequate method of preventing thrombosis and embolism<sup>3</sup> but the reasons for this confidence are not entirely clear. It probably is a satisfactory way of dealing with thromboses limited to the lower legs<sup>4</sup> but one is entitled to suspect that the surgeon can seldom be sure that the ligatures are always placed proximal to the danger zone,<sup>5</sup> and there is some reason to believe that the ligature itself induces thrombosis central to it.<sup>6</sup> Pulmonary embolism has occurred in 5 per cent of cases following bilateral ligation of the superficial femoral veins<sup>7</sup> and in an effort to control detachment of clots from the vena profunda femoris, ligation of the common iliac vein has been advised.<sup>8</sup> It is not within the province of this paper to evaluate the relative merits of the various operations but the principle involved seems to lead to the conclusion that the only vessel which can be ligated with confidence is the inferior vena cava.<sup>9</sup> This seems too radical a procedure except in cases of suppurative pelvic thrombophlebitis.<sup>10</sup>

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The staunchest advocate of venous ligation<sup>3</sup> writes that interruption of the superficial femoral vein is an effective method of treatment but that "Patients with continued infarcts following this procedure should have anticoagulant therapy. Those with continued pain and swelling . . . should be treated by lumbar sympathetic procaine blocks." These qualifications seem to bespeak a lack of total confidence in the surgical treatment and to justify consideration of certain chemical methods now available.

Objection to the use of anticoagulants has been voiced by DeBakey,<sup>11</sup> and it is certainly hazardous therapeutics to treat one disease by substituting another. A very large number of patients has been treated with consistently impressive results, however. No discussion of the many favorable experiences with heparin can be given here.<sup>12, 15</sup> Barker and associates,<sup>16</sup> who gave dicoumarin to 1000 patients postoperatively, reported one embolic death and that was in a patient whose prothrombin time had been allowed to return to normal. Barker<sup>17</sup> gave the drug to 180 patients with pulmonary embolization; only 1.1 per cent of these had subsequent infarction with a 0.6 per cent mortality rate whereas a control group of 678 patients exhibited a 43.8 per cent incidence of recurrence and a mortality rate of 18.3 per cent. Levan<sup>18</sup> noted recurrence of slight superficial thrombophlebitis in only one of 60 cases. Murray<sup>6</sup> found no instance of thrombo-embolism in 400 "dicoumarinized" postoperative patients; 149 patients with pulmonary embolism were treated without a death and 371 cases of peripheral venous thrombosis were managed without pulmonary embolization and with a lower incidence of postphlebotic edema and varicosities. Under conservative treatment Jorpes<sup>15</sup> had a 16 per cent mortality rate in 543 cases of disease of the peripheral vein but anticoagulant therapy (heparin and dicoumarin) applied to 900 patients reduced the mortality rate to 0.67 per cent. In a summary of a very large experience with heparin in Sweden (there is no reason to think that

essentially similar results might not be obtained with dicoumarin) Zilliacus<sup>14</sup> demonstrated a mortality rate of less than one tenth of that in conservatively treated cases; 21 of 65 patients with pulmonary embolism treated non-specifically died, but there were no deaths in 103 heparinized patients. Bruzelius<sup>19</sup> reduced the mortality rate of thrombo-embolism to one-third by using dicoumarin and the postoperative death rate of pulmonary embolism from 0.49 per cent to 0.16 per cent. Allen,<sup>20</sup> who gave dicoumarin to 1628 surgical patients saw a dramatic reduction in the incidence of thrombo-embolism.

This list is by no means complete but it shows what can be achieved. It no longer seems necessary to choose *between* venous ligation and anticoagulant therapy; one supplements the other and judicious combination of the two should provide almost complete protection. Venous ligation appears to be unnecessary in cases of acute non-suppurative thrombophlebitis; dicoumarin gives far better results and lumbar sympathetic block with procaine hydrochloride may also be profitably employed if vasospasm co-exists. Obviously, however, blocks cannot be repeated during administration of dicoumarin for fear of hemorrhage. The patient with phlebothrombosis deserves the double protection offered by venous ligation and anticoagulants. Although it obviously is neither feasible nor necessary to give dicoumarin to every patient who takes to bed because of illness, its prophylactic use in persons over 40 years of age who face a period of immobilization and who present no contraindications should be seriously considered. Allen, Linton and Donaldson<sup>21</sup> noted that a rough similar plan resulted in the "dicoumarinization" of 16.5 per cent of 985 surgical patients and a lowering of the incidence of thrombosis and embolism to about 25 per cent of a control series.

#### THROMBO-EMBOLISM OF CARDIAC ORIGIN

*Coronary thrombosis:* It has long been known that the chambers and valves of the heart are occasionally a source of emboli but the frequency of this event is not :



widely appreciated as it should be. The incidence of mural thrombi in myocardial infarction is especially high, the estimates ranging from 17 to 83 per cent.<sup>22, 32</sup> The frequency with which portions of these thrombi detach themselves and cause clinically detectable disturbances in either side of the circulation is difficult to estimate. Blumer<sup>27</sup> reported that 50 per cent of his patients had mural thrombi and that in 14 per cent of these emboli were clinically detectable. Bean<sup>29</sup> noted that 75 per cent of patients with mural thrombosis of the right ventricle had pulmonary embolism but that fatalities were due to large emboli arising from clots in the pelvis and legs. Nay and Barnes<sup>31</sup> estimate that the incidence of pulmonary embolism in clinical series of coronary occlusion is 3 per cent and, in post-mortem series, 42 per cent. Pulmonary embolism accounts for from 5 to 11 per cent of the deaths which occur in the convalescent period.<sup>28, 29, 33</sup>

Final decision regarding the efficacy of anticoagulants in the prevention and treatment of this form of thrombo-embolism must be postponed, but encouraging experiences have been reported. Although dicoumarin might be expected to prevent extension of the original coronary thrombus or recurrence elsewhere in the coronary tree, its chief usefulness is in the prevention of mural and peripheral venous thrombosis. Solandt and Best<sup>34</sup> reported that heparin could prevent mural thrombosis experimentally but dicoumarin is the drug of clinical choice since Mallory<sup>35</sup> showed that mural thrombi do not form until the sixth postinfarction day and that such clots are organized probably by the sixteenth day. An additional argument for its use rests upon the claim that there is a tendency toward hypercoagulability of the blood in coronary occlusion<sup>36, 38</sup> and during the administration of digitalis<sup>39, 43</sup> and xanthine derivatives.<sup>44</sup> The changes are at best not striking, and large doses of aminophylline given to man have produced no significant alterations in the prothrombin time.<sup>45</sup> The effect of digitalis on the prothrombin time has not been confirmed.<sup>46</sup>

No attempt has been made to assemble all the cases of patients with myocardial infarction who have been treated with anticoagulants. The first report was that of Nichol and Page,<sup>32</sup> who treated 50 attacks in 44 patients with an immediate mortality rate of 16 per cent but in their six autopsies they noted no mural thrombi or emboli. Peters, Guyther and Brambel<sup>38</sup> reported a series of 50 "dicoumarinized" patients with an immediate mortality rate of 4 per cent and a 2 per cent incidence of clinical embolism as opposed to a control group of 60 cases in which the mortality was 20 per cent and the incidence of embolism 16 per cent. Wright<sup>47</sup> reported favorable experience with 76 patients but gave no figures. Parker and Barker<sup>48</sup> used dicoumarin alone or in combination with heparin in the management of 50 patients with acute myocardial infarction; the mortality rate was 10 per cent and the incidence of thrombo-embolism was only 4 per cent.

*Auricular fibrillation:* The occurrence of embolism from detached auricular thrombi is unpredictable<sup>35</sup> and no evidence proving that anticoagulants will diminish the hazards has been published.

*Congestive heart failure:* No studies on the effect of anticoagulants upon the incidence of thrombo-embolism in congestive heart-failure not due to myocardial infarction have appeared but there is no apparent contraindication to their use and every likelihood that good results will be achieved.

*Bacterial endocarditis:* It is now thought unwise to use anticoagulants in this condition because of the accompanying capillary fragility and the tendency to spontaneous hemorrhage.

#### MISCELLANEOUS CONDITIONS

*Cerebrovascular disease:* Young<sup>49</sup> has advocated dicoumarin in the management of patients with hypertensive encephalopathy, cerebral arteriosclerosis and cerebral thrombosis but this appears to be dangerous. Dicoumarin should always be used cautiously in patients with hypertension and it is notoriously difficult to differentiate clinically between small hemorrhages and thromboses in the brain. The drug is probably useful in the treatment of thrombosis.

of the larger intracranial veins, however. Its application to multiple sclerosis does not look promising.<sup>50, 51</sup>

*Hypercoagulability of the blood:* Dicoumarin might be useful in controlling the tendency to thrombocytosis which commonly occurs in patients with leukemia, Hodgkin's disease and polycythemia vera, and following splenectomy but no studies of statistical value are available. Carcinoma of the body of the pancreas is another condition frequently associated with peripheral thromboses. Preliminary studies are also underway concerning the usefulness of anticoagulants in the management of thromboangiitis obliterans, arteriosclerosis obliterans, frost-bite, trench foot and arterioembolism of the extremities.

#### DOSAGE AND ADMINISTRATION

There is no standard schedule for administration of dicoumarin since patients vary in body weight and in sensitivity to the drug. Enough must be given to maintain the concentration of prothrombin in the blood between 10 and 30 per cent of normal.<sup>21</sup> Daily estimations of prothrombin time by a reliable method are imperative, and treatment must not be started until this value is known. When normal, the initial dose is 300 mg. by mouth and 200 mg. is given on the following day. No more is given until the prothrombin time for the day is known. On each subsequent day that the plasma prothrombin concentration is 20 per cent or more, a single dose of 200 mg. is given but none is given if it is less than 20 per cent. The maintenance dose may vary from 100 to 300 mg., however, since individuals may differ in sensitivity. The drug has a delayed action of from 24 to 48 hours and hyperprothrombinemia may persist for many days after its use has been discontinued. Patients with cardiac disease are said to be hypersensitive and smaller doses may be required.<sup>46</sup> The strictest laboratory control is essential if hemorrhage is to be prevented.

#### COMPLICATIONS

The only important danger from use of anticoagulants is hemorrhage. Aggeler<sup>52</sup> collected 1471 cases in which hemorrhagic death due to dicoumarin occurred in 0.34

per cent and less important hemorrhage in 8.3 per cent; the latter figure, however, included many cases of microscopic hematuria, which is not in itself an indication to discontinue using the drug and also cases in which the prothrombin time had been allowed to drop below 10 per cent. Of the 50 patients treated by Peters, Guyther and Brambel<sup>38</sup> the only evidence of bleeding was microscopic hematuria in three. Evans<sup>53</sup> reported two hemorrhage deaths in 56 patients and an incidence of spontaneous bleeding in 14 per cent. Bruzelius<sup>19</sup> found that 4.8 per cent of 1656 patients bled but only half of them importantly, and there were two deaths in this large series. Barker and associates<sup>16</sup> saw major bleeding in 2.5 per cent of 1000 patients, minor bleeding in 3.9 per cent. Geftter, Kramer and Reinhold<sup>54</sup> had eight cases of mild hemorrhage and no deaths in 30 cases. Minor hemorrhage (epistaxis, hematuria, petechiae and ecchymoses) occurred in 3.1 per cent and major hemorrhage in 1.9 per cent of Allen's large series.<sup>20</sup> In the series of 50 cases reported by Parker and Barker<sup>48</sup> the prothrombin concentration was difficult to control in 36 per cent of the patients and three of them exhibited minor hemorrhages. Bleeding due to dicoumarin may be controlled by the transfusion of blood and the intravenous administration of menadione bisulfite in doses of 50 to 100 mg. every four hours until the prothrombin concentration of plasma is restored to 30 per cent or more. All potent drugs are dangerous in inexperienced or careless hands and dicoumarin is certainly no exception, but its controlled use is perfectly justifiable.

#### CONTRAINDICATIONS

There are certain conditions which definitely preclude full dosage schedules of dicoumarin: (1) Blood dyscrasias accompanied by purpura are obvious contraindications; (2) hepatic disease must be approached cautiously if it is accompanied by prothrombin deficiency; (3) renal insufficiency of any degree means that the elimination of dicoumarin will be retarded and its effect therefore cumulative; (4) subacute bacterial endocarditis is not a suitable disease for anticoagulant therapy since



spontaneous hemorrhages are a common feature; (5) ulcerative lesions and recent operative wounds are apt to bleed; (6) patients who are being treated with drainage tubes at various sites are likely to bleed at points of mechanical pressure; (7) recent operations on the brain or spinal cord must be regarded with caution because minute areas of hemorrhages are apt to produce serious disturbances; (8) it would appear unwise to give the drug to pregnant or parturient women.

## CONCLUSIONS

Dicoumarin is an effective but potentially dangerous agent in the prevention of intravascular thrombosis and embolism. It is useful to the surgeon as an adjunct in the prophylaxis and treatment of thrombophlebitis and phlebothrombosis. It should be employed by the internist whenever the tendency to thrombosis is increased because of enforced bed rest, general debility, certain blood dyscrasias or heart disease.

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## A REVIEW OF CERTAIN ASPECTS OF THE PATHOLOGIC PHYSIOLOGY OF HEART DISEASE

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NEW ORLEANS

In view of the greatly renewed interest in congenital heart disease and in the mechanism of congestive heart failure, it is felt that a review of some features of the abnormal physiology involved in these conditions would be timely. Of especial interest are the data collected from direct catheterizations of the right side of the heart. The investigators in this field have contrib-

uted immeasurably to a more lucid understanding of the hemodynamic conditions present in various congenital anomalies and in congestive heart failure. The four congenital diseases of the heart (only ones discussed) in which most of the observations have been made are: (1) patent ductus arteriosus; (2) interauricular septal defect; (3) interventricular septal defect, and (4) the tetralogy of Fallot.

Of considerable importance are the changes occurring in the lungs and pulmonary circulation. These abnormalities in pulmonary dynamics are manifested mainly by: (1) alterations in the blood pressure in the pulmonary artery, veins, and capillaries; (2) chronic pulmonary congestion; (3) acute pulmonary edema; (4) cardiac dyspnea; (5) alterations in vital capacity, and (6) alterations in intrapleural pressure.

### CONGENITAL HEART DISEASE

*Patent ductus arteriosus:* Normally, at birth, every infant possesses a patent ductus arteriosus, but in most instances the lumen gradually is occluded, so that by the end of the second or third month the only remaining vestige is a thin fibrous cord which, from that time on, serves no useful function. Not infrequently, however, the ductus fails to involute and persists as a short patent tube between the descending aorta and the pulmonary artery; this anatomic abnormality has deleterious physiologic effects on both the pulmonic and systemic hemodynamics. When a patent ductus arteriosus obtains, there is a marked difference in the output of each ventricle: the right ventricle receives blood only from the right auricle, which has previously received the same from the systemic circulation via the superior and inferior venae cavae; the right ventricle ejects its column of blood into the pulmonary artery, which already is partially filled with blood entering it from the patent ductus; after traversing the pulmonary circuit, the blood is received by the left ventricle from the left auricle and ejected into the ascending aorta, only to have a part of it "drained off" by the patent ductus and shunted into the pulmonary artery; thus, the output of the left

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ventricle amounts to that quantity put out by the right ventricle plus the additional amount carried via the patent ductus arteriosus.

In order to obtain more definite information regarding the circulatory changes in the pulmonic and systemic circulation resulting from this congenital anomaly, Eppinger, Burwell, and Gross<sup>1</sup> created an artificial ductus in each of five dogs by the surgical anastomosis of the left subclavian artery to the main pulmonary artery. This afforded them opportunity to procure samples of blood: (1) that came directly from the right ventricle; (2) that went into and out of the lungs, and (3) that was ejected into the aorta from the left ventricle. Data received were applied to the Fick principle so as to determine the output of each ventricle. It was calculated that in each of the five dogs the amount of blood shunted back into the pulmonary circulation from the aorta via the ductus was more than 50 per cent of the total quantity of blood put out by the left ventricle; it is obvious at once that the systolic outflow of the dogs' left ventricles was over twice that of their right. To illustrate, data from one of their dogs are as follows:

Output of each ventricle in intact animal—2.05 liters per minute.

Output of left ventricle with shunt—2.83 liters per minute.

Output of right ventricle with shunt—1.36 liters per minute.

Volume shunted from aorta to pulmonary artery—2.83 minus 1.36 = 1.47 liters per minute.

Per cent of output of left ventricle shunted =  $1.47 \times 100 = 51.9$  per cent.

2.83

Then too, it was found by chemical analysis that the mixed blood (from both right ventricle and ductus) going into the lungs was significantly higher in oxygen content than that coming alone from the right ventricle; this substantiated the previously held assumption that a patent ductus resulted in an arteriovenous shunt, with the direction of flow from aorta to pulmonary

artery. Furthermore, by use of water manometers, the authors measured the pulmonary arterial pressures in three of their five dogs, both before and after creation of the artificial ductus; they observed that in two of the dogs the pressures were significantly elevated following the anastomoses. Measurements of blood volumes in the operated dogs revealed increases in two of them; in one instance the blood volume before was 1975 c.c., and 3880 c.c. subsequent to operation.

In addition to their work with experimental animals, Eppinger et al. collected data on six patients, each with a patent ductus arteriosus uncomplicated by other congenital defects; each patient underwent surgical ligation of the ductus. Using methods comparable to those above, they found that the amount of blood shunted through each ductus varied from 45 to 77 per cent of the quantity ejected with ventricular systole; therefore, the left ventricular output was varied directly with the diameter of the ductus, the smallest of which was 7 mm. Other observations of interest included: (1) low diastolic and unusually high pulse pressures in all patients; (2) increased circulation time and total blood volume in each of two patients, and (3) no significant variations in venous pressures or vital capacities.

It can be seen, therefore, that the left side of the heart suffers most of the indignities imposed by a patent ductus arteriosus, the increased amount of work it must perform being proportional, roughly, to the size of the arteriovenous shunt. But the right ventricle is not immune altogether: during ventricular diastole, when the pulmonary valves are closed, blood is pouring into the pulmonary artery from the patent ductus (assumption based upon the diastolic component of the continuous murmur heard in most cases of patent ductus); this may result in an elevation of pulmonary arterial pressure, and during the next systole the right ventricle has more difficulty in opening the pulmonary valves. But this bit of additional work which may result is in no way comparable to that done by the left side of the heart, and this is borne out clinically,

since, as determined by roentgenography and fluoroscopy, left-sided enlargement usually exceeds right-sided enlargement.

Morphologic changes also occur in the pulmonary vessels. One frequently can detect, by fluoroscopy, an increase in the size of the main pulmonary artery and/or its large branches, due possibly, to three factors: (1) chronic elevation of intrapulmonary arterial pressure secondary to an almost constant inflow of blood from the aorta via the patent ductus; (2) continuous bombardment of the walls of the pulmonary artery by a stream of blood from the ductus, and (3) chronic intrapulmonary capillary hypertension secondary to increased venous pressure following left-sided failure, if it can be assumed that left-sided failure of necessity results in increased venous pressure. Due to the abnormally large volume of blood transmitted by the main branches of the pulmonary artery, increased pulsations of these branches upon fluoroscopic examination are often noted and, in addition, a so-called "hilar dance," seen as a pulsating systolic dilatation of the smaller vessels in the root of each lung.

Bloomfield et al.<sup>2</sup> were the first to study directly, by use of the intracardiac catheter and a Hamilton manometer, the right heart pressure in normal subjects. They found that the mean right auricular pressure, with respect to atmospheric pressure, varied from minus 2 to plus 2 mm. mercury, that the maximum systolic pressure in the right ventricle varied from plus 18 to plus 30 mm. mercury, with an average of 25 mm. mercury, and the diastolic from minus 7 to plus 2 mm. mercury. Recently, Hickam and Cargill,<sup>3</sup> by means of intracardiac catheterization, made manometric determinations of pulmonary arterial pressures in normal subjects before and after moderate exercise, and found no significant changes in pressures as a result of exercise; they concluded that the pulmonary circulation can accommodate efficiently to moderate increases in blood flow without increasing the mean pressure. Dexter and Burwell<sup>4</sup> report a case of patent ductus ar-

teriosus in a three-year old female child in whom the right ventricular pressure was 54/1 mm. mercury, and the pulmonary arterial pressure was 55/39 mm. mercury. As far as I have been able to determine, this is the only case of patent ductus so far reported in the literature wherein intracardiac catheterization was made to accurately determine the pressures. Cournand<sup>1</sup> states that the average normal systolic pressure in the pulmonary artery is 25 mm. mercury (identical with the average normal systolic pressure in right ventricle), and the average normal diastolic pressure 8 mm. mercury. It can be seen, then, that in the case cited above the patent ductus led to a marked increase in both the systolic and diastolic pressures in the pulmonary artery.

*Interauricular septal defect:* In most cases where there exists an abnormal communication between the left and right auricle, the opening is quite large and allows a considerable quantity of blood to be shunted from left to right—an arteriovenous shunt; this usually results in tremendous enlargement of the right auricle, right ventricle, and pulmonary arterial tree, since these structures are handling a greatly increased volume of blood. Whereas, it had been a clinical assumption that the flow of blood was from left to right, Brannon et al.<sup>5</sup> proved that such is the case in interauricular septal defects after studying four patients, in each of whom the diagnosis was made clinically. They found that the oxygen content of the right auricular blood was far in excess of that found in blood from both venae cavae, thereby indicating that oxygenated blood was actually flowing from the left to the right auricle. The amount of blood passing through the shunt varied from 52 to 71 per cent of that quantity received from the lungs by the left auricle, and in all cases the output of the right ventricle was over twice that of the left ventricle. In two cases the systolic right ventricular pressure was determined and found to be 40 and 41 mm. mercury. Richards<sup>6</sup> reports a case of interauricular septal defect in which the right ventricular pressure was 59/6 mm. mercury, and the pulmonary ar-



terial pressure 33/10 mm. mercury, the former is over twice the normal, while the latter is only slightly above the average normal value.

*Interventricular septal defect:* Whenever there is a defect in the interventricular septum, the output of the right ventricle is more than that of the left, if the theory of a left to right shunt is correct; it not only ejects all the blood returning from the systemic venous circulation delivered to it by the left ventricle, but also that amount forced into it from the left ventricle via the defect. Baldwin et al.<sup>7</sup> did intracardiac catheterizations on two patients with interventricular septal defects and found that the oxygen content of the blood in the right ventricle was significantly higher than that of blood in the right auricle in each case, indicating a flow of oxygenated blood from left to right. In one case, the right ventricular systolic pressure varied from 33 to 43 mm. mercury, the diastolic from 16 to 10 mm. mercury; in the other case, the right ventricular systolic pressure varied from 54 to 47 mm. mercury, the diastolic from 25 to 20 mm. mercury, thus exceeding the average normal value of 25/2 mm. mercury. The pulmonary arterial pressures were not measured, but it seems logical to think that they too would have been abnormally elevated, for Richards<sup>6</sup> cites a patient with an interventricular septal defect in whom the right ventricular pressure was 74/7 mm. mercury, and the pulmonary arterial pressure 74/25.

*Tetralogy of Fallot:* In this congenital anomaly there is a stenotic pulmonary artery, an interventricular septal defect, and a dextraposed aorta overriding both the left and right ventricle; this set of anatomic changes places a strain upon the right ventricle leading to its enlargement; it is the most common congenital cardiac defect producing cyanosis in adults and children over one year of age.<sup>8</sup> Since a large quantity of the venous blood that is ejected by the right ventricle and passes directly into the overriding aorta without going to the lungs to be oxygenated, one would not expect the pressure in the diminutive pulmonary ar-

tery to be elevated, but to be either normal or decreased. Richards<sup>6</sup> reported observations made in a case of tetralogy of Fallot: the pressure in the "free" portion of the right ventricle was 98/1 mm. mercury, while that in the underdeveloped infundibular portion was only 13/4 mm. mercury, upon passing the catheter into the stenosed pulmonary artery the pressure was found to be 12/8 mm. mercury, and in the left branch 18/10 mm. mercury.

#### COMPENSATED ACQUIRED HEART DISEASE

Even before frank congestive left heart failure occurs in patients with valvular heart disease, or yet prior to the appearance of any clinical symptoms which might make one suspect incipient failure, certain changes in cardiac function may be brought forth by special procedures. Stewart et al.<sup>9</sup> studied 40 patients with various types of the common valvular disorders not in failure along with 13 normal subjects as controls. They found an average decrease in both the cardiac index (cardiac output per square meter of body surface) and in the average stroke volume per kilogram in those patients with valvular heart disease as compared to the controls. This might infer that already increased pulmonary resistance, secondary to early pulmonary capillary congestion, was present, thereby causing a decrease in the amount of blood flow to the left ventricle. In fact, they found a slight increase in the arm to tongue circulation time in the majority of their cardiacs. Bloomfield et al.<sup>2</sup> studied a case of rheumatic heart disease with mitral insufficiency and stenosis, and aortic and tricuspid insufficiency, both during failure and after compensation had been established. By right heart catheterization, they noted that even after failure was overcome clinically, the right ventricular systolic pressure remained abnormally high—57 mm. mercury; normal 25 mm. mercury. They feel that this persistent elevation of pressure may result from continued inefficiency of the left auricle with subsequent pulmonary vascular hypertension, plus the effects of arterial thickening, arteriolar sclerosis and necrosis, and increase in collagen through-

out the interstitial tissue of the lung, which Parker and Weiss<sup>10</sup> believe to be characteristic pulmonary changes in mitral stenosis. Bloomfield et al.<sup>2</sup> noted that no abnormality in pulmonary dynamics occurred in patients with uncomplicated arterial hypertension who did not exhibit clinical congestive heart failure.

#### CONGESTIVE HEART FAILURE

The alterations in pulmonary dynamics occurring with, or as a result of, the clinical syndrome of congestive heart failure are primarily dependent upon congestion in the pulmonary capillaries. It is pertinent, therefore, to discuss here the anatomic changes in the lung parenchyma associated with, and the physiologic effects of, pulmonary congestion.

*Anatomic changes in the lung parenchyma:* The degree of pulmonary congestion roughly parallels the severity of the cardiac failure as judged by the physical signs and symptoms accompanying the condition. In the earliest stages of left congestive failure there may be only dilatation and engorgement of the lung capillaries without clinically detectable edema. Lambert and Gremels,<sup>11</sup> by electrical methods, can detect the occurrence of this pre-edematous stage. If the pulmonary congestion progresses, pericapillary edema ensues, and enough fluid leaks into the alveolar spaces to give rise to clinically apparent fine, moist rales. If a patient develops congestive heart failure severe enough to cause death, then at the autopsy table marked changes in the lung will be seen. Harrison<sup>13</sup> states unequivocally that all such patients invariably exhibit congestion and engorgement of the lungs; such lungs are enlarged, swollen, and heavy with edema fluid, and upon section exude copious amounts of frothy fluid which may or may not be grossly blood-tinged. Upon microscopic examination, one encounters marked capillary dilatation and engorgement, edema of the interstitial spaces, and alveoli which are partially or completely filled by the transudate from the capillaries; the alveoli may show albuminoid casts<sup>14</sup> and large, pigment-containing

"heart-failure cells," in addition to a varying number of red blood cells.

*Physiologic effects of pulmonary congestion:* Once the lungs of a patient in congestive heart failure become the seat of pulmonary congestion, dyspnea ensues, the vital capacity decreases, the normally moderately negative intrapleural pressure becomes more negative, the velocity of the blood flow decreases, and the pulmonary arterial pressure rises.

Dyspnea is often the first clinical evidence of left congestive heart failure, and is frequently the patient's only or major complaint. Just what is responsible for this distressing symptom, and by what mechanism does it appear? By definition, dyspnea is any breathing associated with undue effort whether consciously or subconsciously<sup>15</sup>; only those forms of dyspnea resulting from heart disease—cardiac dyspnea—will be detailed.

In past years it was thought and taught that cardiac dyspnea resulted from the effects of decreased oxygen content and increased hydrogen ion concentration of the blood in contact with the respiratory center, these alterations in the circulating blood supposedly resulting from the inability of the pulmonary capillaries to take on oxygen from, and give up carbon dioxide to, the alveolar air in the presence of an intervening wall of edema fluid. Since this popular and highly attractive theory could not be supported by one shred of concrete evidence,<sup>15, 16</sup> it wavered on its shaky foundations and tumbled into oblivion.

Then how is cardiac dyspnea produced? Legallois,<sup>17</sup> in 1812, first demonstrated that respirations are slowed and increased in depth when the vagus nerves are severed, then Hering and Breuer<sup>18</sup> showed that vagal section inhibited expiratory chest movements normally initiated by the inspiration of air. The Hering-Breuer reflex is of paramount importance in the nervous control of ordinary respiration. Christie<sup>15</sup> states, "There are certain nerve endings in the lungs which act as stretch receptors, and when the lungs are inflated by inspiration, these stretch receptors discharge impulses



which travel to the respiratory center via the vagus nerves which inhibit inspiration, and, at the same time, increase the rate of respiration.” That pulmonary congestion is a direct cause of dyspnea has been proven by numerous investigators.<sup>15</sup> As seen above, the lungs in pulmonary congestion are big and bulky, stiff, taut, and rigid; their alveolar walls are stretched, their air sacs distended with fluid. This marked increase in tension of the lung tissue makes the Hering-Breuer reflex hyperactive; that is, when only a small amount of air is drawn into the lungs, premature impulses pass up the vagi to the respiratory center and cut short the inspiration, and, as a result of this premature initiation of the Hering-Breuer reflex, the respirations are shallow and rapid. To prove that cardiac dyspnea is mainly reflex in origin, many workers, among whom are Harrison et al.<sup>19</sup> have produced experimental pulmonary congestion in animals and noted that the resulting dyspnea is abolished by cutting of the vagus nerves.

Although pulmonary congestion is considered to be the major cause of cardiac dyspnea, there is some evidence that other factors may play contributing roles. For instance, Mills, cited by Hoff,<sup>20</sup> produced transient hyperpnea in normal subjects by first occluding a limb with a cuff, then releasing the cuff; he thinks the hyperpnea due to stimulation of pressoreceptors in the pulmonary vascular bed by the sudden influx of blood from the periphery. Then, experiments performed by Harrison, Harrison and Marsh,<sup>21</sup> later confirmed by Megibow et al., according to Hoff, indicated that perhaps hyperpnea was due to a reflex arising from the great veins and right auricle; these workers induced hyperpnea in animals by inflating balloons in their superior venae cavae and noted the disappearance of hyperpnea upon vagal section. These observations are interesting since elevated venous pressure is a common, though not constant finding in congestive heart failure; however, hyperpnea and dyspnea are not exactly synonymous. Lastly, if heart disease results in a decrease in the oxygen tension of the plasma of the arterial blood

(rarely), the chemoreceptors in the carotid and aortic bodies (located at the bifurcation of the common carotid artery and in the aortic arch, respectively) are stimulated and send afferent impulses via the vagus nerves which result in increase in rate and depth of breathing.<sup>22</sup>

The different clinical types of cardiac dyspnea commonly seen are dyspnea on moderate exertion, orthopnea, and cardiac asthma. Harrison et al.<sup>23</sup> showed that even in normal subjects proprioceptive impulses arising in the active muscles are transmitted to the respiratory center and result in increased breathing. It is well known that exercise increases the venous return, and it is also a fact that the increased depth of breathing, by increasing the negative intrapleural pressure within the thorax, favors venous return. Harrison states this results in an increase in venous pressure in the great veins; if the venous pressure in the cardiac patient is already elevated, then the dyspnea is of a more marked degree than would be seen in a normal individual following a similar amount of exercise.

Orthopnea is that form of dyspnea which is initiated or made worse by assuming the recumbent position. McMichael and Sharpey-Schaefer,<sup>24</sup> using right heart catheterization, proved that the cardiac output of each ventricle is increased upon lying down. In heart failure with the lungs already rigid from edema, the right ventricle must pump more blood into the lungs when the patient becomes recumbent, adding insult to injury by still further congesting the pulmonary tissues and leading to increased dyspnea via the Hering-Breuer reflex. There may be other contributing factors.

Cardiac asthma is that form of dyspnea which usually comes on at night in a patient whose lungs are already congested from heart failure, manifested by the patient's having to sit bolt upright in bed in order better to get his breath, his feeling of extreme suffocation and extreme anxiety, the presence of a chest full of bubbling rales, and, not infrequently, by the hawking up of frothy, blood-tinged sputum. The body position during sleep alone can lead to an

increase in pulmonary congestion; in addition, Harrison<sup>13</sup> thinks that other stimuli arising in various parts of the body may act as "trigger mechanisms" possibly via further increase in venous return and resultant increased right ventricular output in initiating the distressing syndrome; he lists these as: excess heat or cold, alcoholic intoxication, coughing, constipation, abdominal distention, desire to urinate, nightmares, and slipping down in bed.

Patients with left heart failure have decreased vital capacities. Christie and Meakins<sup>25</sup> found that the greater the dyspnea the less the vital capacity, and concluded that the reduction in vital capacity was due to the pulmonary congestion. Since, by definition, the vital capacity is that amount of air which, after the deepest possible inspiration, can be forced out of the lungs on maximal expiration, it is obvious that in dyspneic patients whose inspiratory excursions are cut short, the total amount of air capable of being exhaled is decreased.

Pulmonary congestion affects the intrapleural pressure. The intrapleural pressure during normal breathing at rest varies from about minus 2 to minus 6 mm. of mercury, the pressure becoming more negative upon inspiration—the greater the depth of inspiration the greater the increase in the negativity of the intrapleural pressure. In a patient with congestive heart failure and dyspnea, there is a marked increase in negative pressure which literally sucks more blood up from the periphery into the great veins and into the right heart, resulting in the right ventricle's gushing forth an additional volume of blood into the already congested lung and thereby further increasing dyspnea—a vicious circle is in progress, which if allowed to progress untreated, may result in the death of the patient by drowning in his own lung juice. But the marked increase in negative intrapleural pressure not only increases the venous return, but also may cause distention of the pulmonary capillaries and venous sinuses, which results in a pooling of the blood already present, thereby decreasing the flow through the pulmonary veins to the left ventricle.

Cournand,<sup>4</sup> by means of right heart catheterization, has shown that in normal subjects deep inspiration results in an increased output by the right ventricle and a decreased output by the left ventricle; there is no reason to doubt that such similar effects occur in cardiac dyspnea, and when such obtain, the left heart receives less blood from the lungs than is ejected into them by the right heart, and pulmonary congestion is augmented.

That the velocity of the blood flowing through a congested and distended lung is slowed should be readily seen; a law of biophysics says, in effect, that the speed of flow varies inversely as the cross section of the vascular bed. This is borne out by the clinical observation that the arm-to-tongue circulation time is usually prolonged in cases of pulmonary congestion.

*Pulmonary dynamics in congestive heart failure studied by means of right heart catheterization:* The relatively recent perfection of the technic of slipping a small rubber catheter up the veins of the arm or leg and into the right side of the heart opens up new and fertile fields for the direct observation of not only the many physiologic phenomena inherent in the normal heart cycle, but also the alterations in intracardiac pressure and flow resulting from pathologic changes in the heart.

Although the use of this direct method of approach is still in its infancy, nevertheless, it has yielded some pertinent information regarding hemodynamics in congestive heart failure from various types of heart disease. Bloomfield et al.<sup>2</sup> observed in a patient in congestive heart failure having mitral, aortic, and tricuspid insufficiency on a rheumatic basis, that the mean auricular and right ventricular end-diastolic pressure was 29 mm. mercury and the right ventricular systolic pressure averaged 103 mm. mercury, or approximately four times the normal value; following compensation, the auricular and ventricular end-diastolic pressure returned to normal but the ventricular systolic pressure remained elevated. A patient in failure from arteriosclerotic heart disease had a right auricular



and ventricular diastolic pressure of 10.5 mm. mercury, and a maximum ventricular systolic pressure of 75 mm. mercury. Measurements in a man with decompensated syphilitic heart disease revealed right end-diastolic and high systolic ventricular pressures of 12 and 73 mm. mercury, respectively. In another case of rheumatic valvulitis, the authors recorded the pressures in both the pulmonary artery and the right ventricle: the maximum systolic pressure in the pulmonary artery was identical with that in the ventricle, measuring 83 mm. mercury; the diastolic in the lesser arterial circuit was 25 mm. mercury, or about three times normal. These investigators found that in all cases of left ventricular failure studied, regardless of etiology, the right ventricular systolic and pulse pressures (difference between ventricular systolic and diastolic pressure) were definitely increased. And they feel that an increase in right ventricular pressure points to a similar increase in pulmonary arterial pressure.

Richards<sup>6</sup> presented data on a patient with cor pulmonale, secondary to primary disease in the lung, in which the right ventricular systolic pressure rose to 60 mm. mercury. Figures on a case of mitral stenosis indicated a tremendous hypertension in the pulmonary circulation, as the maximum ventricular systolic pressure reached 120 mm. mercury, and only fell to 50 mm. mercury after clinical compensation was established. In this instance there was an apparent five-fold increase in the vascular bed, and one can see the tremendous importance of pulmonary congestion in left-sided heart failure.

Hickam and Cargill<sup>3</sup> studied pulmonary arterial pressures in patients in congestive heart failure both at rest and after exercise; some had mitral stenosis while others were victims of syphilitic and hypertensive heart disease. They found that the pulmonary arterial pressure was elevated in each patient before exercise and that it increased markedly after exercise; their exact figures are not available.

These studies by the several investiga-

tors indicate that patients exhibiting clinical left-sided heart failure invariably have pulmonary hypertension, as reflected by abnormal elevation of the pressure in the pulmonary artery and right ventricle.

*Pathogenesis of pulmonary congestion:*

If we offer a correct solution to the cause of pulmonary congestion, we will, of course, solve the problem of the pathogenesis of clinical left-sided heart failure, for the dyspnea, orthopnea, and fine moist rales in the lungs present in so-called left-sided failure are due to the pulmonary congestion, as has been shown above. But has there ever been offered a perfectly sound and scientifically proved explanation of pulmonary congestion—that it is due to one solitary factor, or that there are several factors responsible, each of which is consistently altered in a similar manner in every case of left-sided heart failure? Not that I am aware of. But let's follow a case of, say, essential hypertension and see how pulmonary congestion may result. The work that the left ventricle does may be expressed as a product of its output times the peripheral resistance; when the latter is increased by essential hypertension, the left ventricle must work harder to maintain a normal output. As a result of this extra work, the ventricle undergoes hypertrophy and dilatation, but it is still efficient, if its efficiency can be measured by its ability to continue its usual output. A critical point is reached finally, however, when the ventricle cracks and it is physically unable to dispatch all the blood which it receives. It is more or less generally accepted that this inability of the ventricle to fully discharge its contents is the first step toward full-blown left-sided failure.<sup>26</sup> As residual blood accumulates and the left ventricle further dilates, its pressure during diastole rises,<sup>16</sup> making the left auricle's job of passing its blood into the ventricle more difficult; but by hypertrophy and dilatation it performs its task efficiently for a while then, like its partner, it tires and is unable to pass forward all of the blood coming from the lungs. When, as a result of the residual blood in the left auricle, the intra-auricular pressure

risers, and acts as a barrier to the blood coming from the lungs via the pulmonary veins, there must be a damming back of blood into the lungs. To store this blood which the right ventricle puts out but which the left side of the heart is unable to relay, additional capillaries open up throughout the lungs which later dilate as more blood accumulates. These events keep the pulmonary intracapillary pressure from rising too high, but when there are no more capillaries available to absorb the excess blood when the ones in use are dilated to their maximum, then of necessity, there must be an additional increase in intracapillary pressure.

Now, granted that there is increased intracapillary pressure secondary to left auricular failure, is that pressure from this source alone enough to drive fluid across the capillary membrane into the parenchyma of the lungs? Landis and Gibbon<sup>27</sup> showed that fluid will pass out of the capillaries into the tissue spaces if the venous pressure rises above 100 mm. water. But there may be another factor which causes a still further elevation of the intracapillary pressure. It is a fact that most patients in congestive heart failure have an increased blood volume<sup>16</sup>; it is not illogical to reason that the presence of still more fluid in the engorged capillaries further increases the intracapillary pressure up to a point where there occurs transudation of fluid into the lungs, causing pulmonary congestion and the clinical picture of left-sided heart failure.

There have been several explanations as to why the blood volume is increased. Fitcher and Schroeder<sup>28</sup> observed that the renal excretion of sodium chloride was markedly reduced in four patients in congestive heart failure. Warren and Stead<sup>29</sup> conclude that in congestive heart failure there is a disturbance of renal function, as a result of which salt and water are retained in the body and produce an increase in blood volume. Merrill<sup>30</sup> states that Lyons showed that salt and water retention can produce a rise in venous pressure in normal subjects. Grant and Reischman<sup>31</sup> demon-

strated an increase in blood volume, venous pressure, and volume of extracellular fluid in healthy medical students following ingestion of an excess of sodium chloride. So it seems that the retention of salt (the sodium ion in particular) in the body can be a major factor in the production of an increase in blood volume in both normal subjects and in those in congestive heart failure. The details of the theory of the mechanism of sodium retention will not be gone into here; the reader is referred to papers by Fitcher and Schroeder,<sup>28</sup> Warren and Stead<sup>29</sup> and Merrill.<sup>30</sup>

That derangement of salt and water metabolism is a factor of major importance in considering the pathogenesis of pulmonary congestion in heart disease is borne out by clinical observations. Many investigators<sup>20, 29, 30, 32, 33</sup> have found that patients with severe congestive heart failure can be made to lose their gross peripheral and pulmonary edema and become clinically compensated simply by rigid restriction of salt intake and without the use of digitalis; further, once apparently compensated these same patients can be thrown back into heart failure at will by the excessive ingestion of salt and water, even if digitalis is given concurrently; the return of pulmonary and peripheral edema, dyspnea and orthopnea is usually preceded by a rise in blood volume.

In spite of the fact that increased blood volume often accompanies, and commonly even precipitates, the development of cardiac pulmonary congestion, one can by no means say, therefore, that it is the sole or most important cause of this phenomenon. Before marked engorgement and actual pulmonary edema fluid forms, there first must be an increase in pressure transmitted backward from the left auricle to the pulmonary veins and into the lung capillaries; after the stage is set, so to speak, then the additive effect of any increased blood volume in further raising the intracapillary pressure may be sufficient to initiate or increase a transudation of fluid across the capillary walls into the parenchyma of the lung.

Observations made in the course of ex-



perimental work on animals certainly suggests that many types of pulmonary edema, even cardiac, may be partially reflex in origin. Henneman<sup>14</sup> presents an excellent review of the subject of the experimental production of acute pulmonary edema, describing in detail some of the interesting procedures; the data below are taken from Henneman's paper. Antoniazzi produced acute pulmonary edema in rabbits by ligation of the arch of the aorta distal to the origin of the carotid arteries; the edema could not be produced if both vagi were sectioned previously; the central nervous system was easily depressed by hypnotic drugs to a point where no edema resulted after aortic ligation. Luisada, after experimenting with 250 rabbits and producing pulmonary edema by intravenous adrenalin, felt that the edema resulted from a hypertension produced in the carotid and cephalic vessels. The conception that pulmonary edema following phosgene poisoning is due to direct action on the lung capillaries was challenged by the observation that if the vagus nerves were cut previously the classical signs and symptoms were largely prevented. In more recent experiments than those cited by Henneman, Luisada and Sarnoff<sup>34</sup> noted that they could produce acute pulmonary edema in dogs by the rapid infusion of fluid into their common carotid arteries, but could not produce edema when the same amount was injected at a similar rate into the femoral arteries; they found also that if the carotid sinus were denervated, pulmonary edema failed to occur in five out of seven dogs. They believed that ". . . . . the results of experiments on pulmonary edema caused by adrenalin, ligation of the aortic arch and venous infusion, should now definitely focus the attention of students of pulmonary edema upon the nervous system and not upon the myocardium. That either irritation of the myocardium (coronary occlusion), or distention of the heart cavities (heart failure, hypertension) may be one of the causes of pulmonary edema cannot be denied, but we feel that either of these phenomena is secondary to the distention of the large arterial vessels

as a cause of reflexes which favor acute edema of the lungs. For the occurrence of pulmonary edema a condition of distention of the lung capillaries is essential. On this condition, an acute reflex increase of permeability may be superimposed which will lead to paroxysmal pulmonary edema."

#### SUMMARY AND CONCLUSIONS

1. The pulmonary dynamics in some of the more common congenital cardiac anomalies are discussed, including data derived from right heart catheterizations in these conditions.

2. Patients with valvular heart disease have abnormalities of cardiac function which often may be detected prior to the onset of left-sided heart failure.

3. Pulmonary congestion is discussed from the standpoint of pathologic anatomy, pathologic physiology and pathogenesis.

4. Observations on intracardiac and pulmonary arterial pressure changes in left-sided congestive heart failure as recorded by direct right heart catheterizations are reviewed.

5. Patients in right-sided congestive heart failure have hypertension in the pulmonary vascular bed manifested by increased pressure in the pulmonary artery and right ventricle.

6. Pulmonary congestion of cardiac origin depends upon increased pulmonary intracapillary pressure, this resulting primarily from an elevated venous pressure subsequent to failure of function of the left auricle but augmented by an increased blood volume. There is evidence to show that reflexes arising directly from the heart, the great vessels and some of their main branches, may play a very important contributing role in the production of pulmonary edema of cardiac origin.

7. There are probably other factors as yet poorly understood concerned in the production of pulmonary congestion.

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## THE WOLFF - PARKINSON - WHITE SYNDROME (BUNDLE OF KENT SYNDROME; FALSE BUNDLE BRANCH BLOCK)\*

ARTHUR SILVERMAN, M. D.

NEW ORLEANS

When Wolff, Parkinson and White<sup>35</sup> presented the first comprehensive report of this syndrome in 1930, they evoked a world-wide response. The interest in this electrocardiographic pattern has even now not subsided, principally because of the controversy concerning its mechanism and prognosis. The literature abounds with case reports, interpretations and conflicting data and opinions. In this paper I shall attempt to present in a succinct manner the most authoritative and widely-held views and to report a series of cases gleaned from the files of the Charity Hospital in New Orleans.

### DEFINITION

Although cases were reported by Wilson<sup>32</sup> in 1915 and again by Wedd<sup>31</sup> in 1921 and by Hamburger<sup>9</sup> in 1929, it was not until 1930 that a clinical entity was evolved, for at that time Wolff, Parkinson and White<sup>35</sup> collected and reported eleven cases with careful four year follow-ups.

The electrocardiographic tracing is composed of a short PR interval with a widening of the QRS complex in such a manner that the time from the beginning of the P

\*Awarded the prize given by the Professor of Medicine at Tulane University School of Medicine to a Senior student who presented the best thesis on a subject related to internal medicine.



wave to the end of the QRS complex is within normal limits. The PR interval is usually less than 0.1 second and the QRS complex has characteristics suggesting bundle branch block. The ventricular complexes are wide and slurred, and the T waves may be opposite in direction from the main QRS deflection. The most usual type simulates a left bundle branch block, with the initial ventricular complexes as seen in left axis deviation and the T waves in leads I and III in the opposite direction from the main deflection of the QRS complex. If it were not for the short PR intervals, these tracings would be indistinguishable from organic bundle branch block.

#### INCIDENCE

To date, approximately 300 cases have been reported in the literature; obviously the actual number of cases is far greater. Ohnell,<sup>19</sup> in his comprehensive monograph on this subject, reports an incidence of from 0.05 to 0.1 per cent. Boyer,<sup>2</sup> in a review of 2000 tracings of 1356 patients in the Army, reports an occurrence of 0.5 per cent in this group. This phenomenon is usually manifested in the young (second, third and fourth decades), most commonly in the male, perhaps accounting for Boyer's high figures among soldiers.

#### CLINICAL DATA

Frequently the history dates back to puberty, when the patient first began to experience periodic attacks of palpitation after exercise or even at rest, but this finding is not constant. Of the arrhythmias which these patients are prone to develop, paroxysmal, supraventricular tachycardia ranks first; auricular fibrillation occurs with considerably less frequency. Lately, a few cases have been reported<sup>18</sup> in which there were paroxysms of ventricular tachycardia.

In many cases, both the PR interval and the QRS complexes suddenly revert to normal without change in direction or contour of the P waves. This may occur spontaneously or when the heart rate is increased by exercise or atropine. When the heart rate slows, the abnormal characteristics may return. Patients in this group are particularly liable to attacks of paroxysmal tachycardia

during which the ventricular complexes invariably\* assume a normal configuration.

It has been shown<sup>11</sup> that there is a greater incidence of paroxysmal tachycardia in those patients with QRS changes as well as short PR intervals. It is of interest to note that among patients exhibiting the phenomenon of paroxysmal, supraventricular tachycardia, 5 per cent demonstrate a Wolff-Parkinson-White type electrocardiogram, and that conversely among patients recording this tracing 70 per cent are subject to paroxysms of supraventricular tachycardia.<sup>19</sup>

#### MECHANISM

Wolff, Parkinson and White originally suggested that the mechanism was based on increased vagal tone, implying that there is a paradoxical vagal effect with a simultaneous exercise of two diametrically opposed influences, one accelerating conduction between auricles and ventricles with shortening of the PR interval, the other retarding conduction through the bundle of His, giving rise to the lengthening of the QRS complex. This concept is mentioned principally from the historical point of view since it is now usually considered untenable, in the light of recent evidence, by most observers. White, himself, is now supporting the theory of accessory bundle (*v. infra*); on the other hand, Parkinson together with Hunter and Papp<sup>11</sup> hypothesize that the anomalous beat arises near but not within the sinoauricular node, and that the normal ventricular complex is interfered with by a ventricular extrasystole which arises prematurely and low in one bundle branch.

Today, the most widely held, although by no means universally accepted theory is the hypothesis of an accessory pathway of atrioventricular conduction which was first introduced by Holzman and Scherf<sup>10</sup> in 1932 as a possible explanation. Almost simultaneously Wolferth and Wood<sup>33</sup> advanced the same hypothesis which they substantiated

\*Movitt (18) reported a case in which the aberrant bundle (*vide infra*) was evidently able to conduct the auricular impulses during supraventricular tachycardia, leading to preservation of the aberrant QRS complex during the attack.

histologically in 1943.<sup>36</sup> Since this theory is the one for which there is the best supportive experimental data, and the one which lends itself to the clearest thinking in dealing with this phenomenon, we will confine our discussion to it. For a comprehensive survey of all the theories ever promulgated as an explanation of this subject, the reader may refer to Ohnell's monograph on pre-excitation.

More than 30 years ago Kent demonstrated histologically a muscle bundle in the atrioventricular groove which joined the right auricle and right ventricle in man. He termed this structure the "right lateral bundle." Interest in his finding lay dormant until the advent of the electrocardiographic anomaly under discussion, when in 1933 Wolferth and Wood utilized it in explaining the mechanism of this pseudo-bundle branch block.

When in 1933, Wolferth and Wood<sup>33</sup> presented the theory of a functioning, conducting right lateral bundle, they reported nine cases of this syndrome which could not be reverted to normal with exercise or atropine. In presenting their hypothesis they reasoned as follows:

1. The short PR interval is due to the short, direct pathway from auricle to ventricle via Kent's bundle.

2. The premature invasion of the ventricular myocardium by this impulse causes: (a) a slurring of the initial QRS deflection and (b) a widening of the QRS complex at the expense of the PR interval.

3. In some cases, conductivity in the bundle of Kent may not be highly developed. Consequently, when subjected to the passage of impulses at a rapid rate, as during paroxysmal tachycardia, it may fail to function.

4. Kent showed that retrograde conduction in rats was possible under certain circumstances. Therefore, a retrograde impulse might travel from ventricle to auricle at a time when the physiological state of the auricular muscle would favor the inception of an abnormal rhythm. This mechanism might explain the frequency of paroxysmal tachycardia in these people.

5. The assumption of a functioning bundle of Kent does away with the necessity of postulating a lesion or defect in conduction in youthful patients without evident cardiac damage.

6. During both normal and abnormal mechanisms, the duration of the interval from the beginning of the P wave to the end of the QRS complex tends to remain constant. Only one interpretation seems possible; namely, that the variable factor is early aberrant conduction from auricle to ventricle. This does not interfere with conduction through the junctional tissues, but alters the duration and form of the initial portion of the ventricular complex in direct proportion to the prematurity of arrival of the aberrant impulse in the ventricular myocardium.

Then in 1943, these same authors<sup>36</sup> studied a case of typical Wolff-Parkinson-White syndrome in a young boy subject to attacks of paroxysmal tachycardia, but in whom no evidence of heart disease was ascertained. The typical tracing was a constant finding. He died at the age of 16, two hours after an attack of paroxysmal tachycardia.

At autopsy the heart was grossly normal and there was no accountable lesion. They made serial sections about the atrioventricular groove beginning just to the right of the aorta. In this manner they demonstrated a muscle bundle leaving the auricular muscle and joining the ventricular muscle after passing by means of a bridge of tissue across the ventricular cavity just below the attachment of the tricuspid valve. They demonstrated in this patient's heart three such accessory connecting bridges of muscle tissues between the right auricle and right ventricle, these connections being of the type which should be able to conduct an impulse from auricle to ventricle. This study supports the hypothesis of accessory pathway conduction. Proof would require direct evidence that these tracts are capable of transmitting the excitatory process. The question of the incidence of these accessory bundles is also unanswered.

Further substantiating evidence for this



theory is recorded by Rosenbaum, Hecht, Wilson and Johnston<sup>24</sup> wherein they show that the form of the ventricular complex in unipolar leads from the esophagus, precordium and other points on the thorax suggests that in these cases the dorsal wall of the ventricles is activated prematurely by impulses of supraventricular origin. They also find evidence that the atrioventricular node and bundle continue to function normally in this condition. They also note that the anomalous ventricular complex assumes the normal form when the pacemaker shifts to the lower levels of junctional tissue. These observations support the view that impulses pass from the auricles to the ventricles not only by the normal route but also by one or more additional channels.

Finally, the work of Butterworth and Poindexter<sup>3</sup> should not go unmentioned. They demonstrated that a typical Wolff-Parkinson-White pattern could be reproduced in animals by the artificial introduction of a short circuit comparable to the right lateral bundle, lending further support to the hypothesis of premature aberrant conduction.

In short, then, there are good experimental data and clinical observations to point out that accessory pathway conduction is the probable mechanism at work here. At any rate it offers the most satisfactory working hypothesis.

#### PROGNOSIS

What do we tell the patient in whom a Wolff-Parkinson-White syndrome is demonstrated? Is it necessary to say anything, or are we dealing with a phenomenon of no clinical significance? Indeed, we are faced with the dilemma of perhaps creating a cardiac neurosis, once established difficult to dislodge, or on the other hand of performing an injustice to the patient by not informing him of a hazard to his chance for a long life. My only contribution to this problem must be that of faithfully recording both sides of the controversy.

Lynch and McAllister<sup>16</sup> present the view that we are dealing with a functional phenomenon and that the patient is suffering from an electrocardiogram rather than a

disease. They would ignore the finding and give the patient complete assurance for life and unrestricted activity on the basis of the cardiac status of the moment.

Bishop<sup>1</sup> along the same line of thought brings up the argument that when heart disease is an associated finding with the syndrome it is of such diversified forms that it is hardly conceivable that the organic heart disease when encountered is more than coincidental. He reiterates the common observations that exercise does not seem to increase the frequency of the attacks, for they may well occur at rest and that apparently, a small percentage of patients seem to outgrow their "electrocardiographic difficulty" without first decreasing their activity.

Boyer,<sup>2</sup> relating his Army experience with this problem, finds only an abnormally increased incidence of psychoneurosis in these patients, emphasizing, of course, the importance of caution when offering these patients a guarded prognosis.

On the other hand are the many reports of the association of this pattern with such entities as active rheumatic heart disease, aortic regurgitation, mitral stenosis, hypertensive heart disease and thyrotoxicosis.<sup>11, 28</sup> Master, Joffes and Deck<sup>17</sup> report a case with thyrotoxicosis without heart disease in which the pattern reverted to normal after thyroidectomy.

In referring to this syndrome in an address<sup>37</sup> to a group of insurance medical directors, Frank Wilson remarked that he did not consider this condition trivial. He recounted one patient who had died with prolonged tachycardia, and at autopsy definite evidence of myocardial change was found.

Fox<sup>7</sup> suggests that it is conceivable in the older age group that a circulatory difficulty of the A-V node due to coronary sclerosis may sufficiently depress its functional activity to permit the aberrant mechanism to take over some of the conducting function.

Kimball and Burch<sup>13</sup> have collected six deaths from the literature and reported two more cases among which at least five were attributed to paroxysmal tachycardia associated with the Wolff-Parkinson-White

syndrome. Three other deaths were said probably to be due to paroxysms of tachycardia in patients with a typical picture of the syndrome. Their opinion is that the Wolff-Parkinson-White syndrome should be regarded as strongly suggestive of definite evidence of heart disease. They suggest that a guarded prognosis be discussed with a responsible member of the family rather than with the patient in order to avoid precipitating a cardiac neurosis.

THE WOLFF-PARKINSON-WHITE SYNDROME IN THE  
CHARITY HOSPITAL IN NEW ORLEANS

In an attempt to determine how a local series of patients manifesting the Wolff-Parkinson-White electrocardiogram would correlate with the data accumulated in the literature, I selected patients who had been reasonably well worked up and from whom at least one typical tracing had been recorded. There were ten known patients of this description in the files of the Charity Hospital record library.

*Incidence:* All but one of these patients were between the ages of 19 and 55 years and 60 per cent (six patients) were less than 37. There were eight white patients, two colored patients, six females and four males. One colored patient was a male and the other a female.

*Heart Disease:* Two patients had no determinable evidence of heart disease. Another patient probably had some cardiac changes as the only typical tracing was obtained when she was in profound uremia which terminated fatally two months later. It is not known whether or not a fourth patient had heart disease, as the typical tracing was recorded as a routine procedure before metrazol shock therapy was instituted for hebephrenic schizophrenia.

The other six patients had definite evidence of organic heart disease. It is well to bear in mind at this point that these tracings were not recorded routinely, but rather ordered in patients in whom a determination of cardiac status was indicated for one reason or another. For example, in this group of patients there were five hypertensives, three patients with definite signs of failure, and four patients with enlarged hearts. Therefore, the presence or absence

of heart disease in these patients is not very significant. However, the types of heart disease encountered is important. That is to say, we would like to know if this electrocardiographic tracing is common to any particular type or group of heart diseases. Accordingly, a resumé of these cases and the type of heart disease occurring in them becomes essential.

1. A young, white male suffered a metapneumonic empyema in 1935, complicated by purulent pericarditis which was drained, leaving him with an adhesive pericarditis. Five years later two typical Wolff-Parkinson-White tracings were recorded. These were found to be of a normal mechanism, but recorded at a time of a much higher pulse rate. In the five year interval he suffered six attacks of paroxysmal tachycardia and occasional bouts of dyspnea on exertion, but no other difficulties.

2. A young colored male was in the psychiatric ward with a diagnosis of hebephrenic schizophrenia. A routine electrocardiogram revealed the anomalous tracing. It was regarded as normal and no further cardiac studies were made. It is not known whether he suffered attacks of tachycardia.

3. An elderly white female had hypertension, dyspnea, orthopnea, ankle edema, tachycardia, precordial pain and an enlarged heart. She actually developed a paroxysm of tachycardia while on the ward. Her tracing was somewhat equivocal in that the PR interval was somewhat longer than that usually seen. There was no repeat tracing.

4. A 37 year old white female was a diabetic with hypertensive cardiac disease. She had an enlarged heart, weakness, dyspnea, ankle edema and precordial pain. Her tracing was not completely typical in that the QRS complex was slurred but not of long duration. The PR interval was .1 second, and the heart rate was 121. An earlier tracing had a normal mechanism at a heart rate of 102.

5. A 53 year old white female had a typical tracing recorded while she was in the hospital for management of her diabetes. There was no history of tachycardia or



symptoms of heart disease, nor was there any evidence of heart disease by physical examination.

6. A 55 year old white male had severe hypertensive, arteriosclerotic heart disease. He had many admissions into the hospital for congestive failure. He was in auricular fibrillation for two months, finally returned to a normal mechanism and was discharged. A year and a half later he was admitted again in congestive failure when an electrocardiogram was taken. The tracing was thought to show Wolff-Parkinson-White patterns in that the PR interval was .13 second and the QRS .14 second with a slurred and notched R<sub>1</sub>. This was the only tracing demonstrating this mechanism.

7. A young white female was admitted for a normal pregnancy. An electrocardiogram was taken because of a history of paroxysmal tachycardia. The tracing was a typical pattern of pseudo bundle branch block. She was normotensive, but had occasional bouts of weakness and orthopnea. She had cardiac enlargement. The tracing was repeated the next day and showed the same mechanism.

8. This patient was another young white female who was in uremia on the basis of malignant nephrosclerosis. One tracing demonstrated a typical pattern of aberrant conduction. The next tracing taken three weeks later showed a normal mechanism. Five weeks later she expired.

9. A 34 year old white male was admitted for multiple injuries sustained in an automobile accident. An electrocardiogram made on that admission was interpreted as supraventricular tachycardia with a heart rate of 240 beats per minute. He was discharged the same day, to return a few days later with evidence of increased intracranial pressure. An electrocardiogram taken on this admission demonstrated a Wolff-Parkinson-White pattern. He had a past history of occasional attacks of tachycardia before his accident. There was no evidence of heart disease.

10. A 55 year old white female had severe hypertensive cardiovascular disease for 12 years. One electrocardiogram showed a

typical Wolff-Parkinson-White syndrome with a 2:1 block. A later tracing showed a return to a normal mechanism. There was no history of tachycardia.

In summary it is noted that in this group of patients a Wolff-Parkinson-White syndrome was associated with four cases of hypertensive heart disease, one arteriosclerotic heart disease, one severe uremia and one patient with adhesive pericarditis.

*Paroxysmal Tachycardia:* There was a history of paroxysmal tachycardia in four of these patients. It is not known whether or not a fifth patient (the schizophrenic) had a history of tachycardia.

Of this group of patients then, we note that there is a high incidence of associated heart disease, especially of hypertensive etiology; this is explained in that this was not a routine series of electrocardiograms, and that hypertension is a common factor in heart disease in the population of which this group of patients is representative. As might be expected, there is a high incidence of paroxysmal tachycardia in the group. The distribution of these patients by age and sex is comparable to that reported by other investigators.

#### SUMMARY

1. The Wolff-Parkinson-White syndrome is defined as the combination of an electrocardiographic pattern of a short PR interval, wide, slurred QRS complex and a normal P-J interval in a young patient who commonly demonstrates paroxysmal tachycardia.

2. The mechanism of this pattern is probably that of accessory pathway atrioventricular conduction with short-circuiting of the excitatory wave. This theory is explained and the evidence in favor of it is presented.

3. The actual significance of this finding is as yet undetermined. Many are inclined to dismiss the syndrome as being without clinical importance, but some reported deaths are herein discussed.

4. A series of cases from the Charity Hospital is reported, and discussed.

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# NEW ORLEANS Medical and Surgical Journal

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## PUBLIC RELATIONS PROGRAM OF LOUISIANA STATE MEDICAL SOCIETY

The Council on Medical Service and Public Relations of the Louisiana State Medical Society recently announced its Public Relations Program for the year 1948. The program comprises eleven major parts and is to be promulgated under the leadership of the Council in cooperation with the Executive Committee and the House of Delegates of the Louisiana State Medical Society

and will serve as a guidepost to the component parish medical societies throughout Louisiana. Dr. A. V. Friedrichs, Chairman of the Council, made the announcement.

By the institution and fulfillment of the program the doctors of Louisiana intend to overcome the propaganda issued by the Government relative to a compulsory system of medical care. Through a program of progressive accomplishments by the medical profession, rather than through a program of expensive propaganda as indulged in by the Government, it is agreed that the doctors have the answer to the proponents of socialized medicine.

One phase of the program, namely, "General Public Relations", provides for the presentation of educational health radio programs, especially in the rural areas of this state. A speakers' bureau is to be established and lay persons and members of the profession will appear before civic clubs, women's clubs, parent-teacher groups, and other interested groups to present educational health talks, talks on economics of medicine, voluntary health insurance, and numerous other subjects.

An educational health column is to be released weekly and it is anticipated that it will appear in all newspapers throughout Louisiana. A news bureau will be established to disseminate pertinent information to the general public relative to the scientific advancements made by the profession and also to advise the general public what the medical profession is doing in their behalf.

Another part of the program is to promote voluntary health insurance. The Louisiana Physicians Service is operating the "Blue Shield" plan, which offers surgical and obstetrical care and is sponsored by the Louisiana State Medical Society. "Blue Cross" hospitalization coverage is also part of the voluntary health program. Through this medium persons who are willing to voluntarily enroll may contribute a monthly fee and thereby prepay the costs of the doctor bill for surgery and hospitalization.

It is proposed that the Medical Society will take leadership and assist in the estab-

lishment of health councils in every parish throughout the state in cooperation with all other voluntary agencies interested in health. Another phase of the program includes a closer working relationship with other health agencies, societies, and civic clubs, and a program and medium to keep cooperating government health agencies adequately informed of voluntary health progress.

The program also includes the institution of a campaign to maintain and enhance patient-physician relations.

In general, the program provides for a medium to maintain adequate medical care at a cost which the patients can afford and at the same time keep medicine a private enterprise.

In times past the position of the physicians and the appreciation of the public left no question as to how medicine should be practiced. Now the doctors have to fight to maintain this position. Active participation by the membership is needed.

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### LOUISIANA

#### PHYSICIANS SERVICE, INC.

A vital contribution of the physicians of Louisiana in the fight against state medicine is the Louisiana Physicians Service, Inc. The Louisiana Medical Society, as does organized medicine in many states, sponsors a voluntary sickness insurance plan which has been in operation since January 1, 1947. This is a necessary part of our plan to meet the criticism that medical care is so expensive that it is inaccessible to the majority. In all of the schemes of the social planners it must still be remembered that the public ultimately pays for medical care regardless of the method by which payment is collected. We wish to continue to show that medicine as a private enterprise, with voluntary insurance, is best.

Securing proper adherence of the public to any plan is largely dependent upon the support which the individual physicians give it. When the physician indicates that he is participating, he renders support to

the profession. Insurance of this type has little statistical experience to guide it. Our organization is courageously furthering the interests of voluntary insurance and necessarily of the individual member. The aim therefore is that all should familiarize themselves with the details, should participate in the surgical agreement and should, above all else, acquaint their patients with the advantages.

There are now 20,351 individuals enrolled on our plan. There are 64 plans in operation over the nation. The Louisiana Physicians Service, Inc. is the 46th in size over the country, having surpassed some 18 plans in growth in the first year. The board and administrators of Louisiana Physicians Service, Inc. are to be congratulated on their achievements thus far. Our own protection depends on our strenuous collective effort.

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### THE BLOOD BANK SITUATION

It is learned that recently the American Red Cross has undertaken a National Blood Bank Program designed eventually to provide blood and blood derivatives to the entire nation without charge for the products. As is usual in matters where nationalization of medicine is in view, the figures are astronomical. The projected plan is to spend \$5,000,000.00 to start the program and \$20,000,000.00 annually; it is reported that 3,700,000 pints of blood must be obtained within the next year—one pint for every 35 Americans.

The American Red Cross, while not politically dominated, operates with government sponsorship; not with tax money but with public subscription. The allotment of blood and its products by the American Red Cross would ultimately lead to the effect of having the Red Cross practice medicine. The transition from this arrangement to state medicine could become an imminent danger.

The physicians who operate the blood



banks of hospitals and communities have formed an association. The association is composed of institutional and individual memberships. Their objective is to pool their knowledge and influence; to render useful and adequate service. It seems fitting in the interest of good medicine and the ultimate welfare of the patient, that operation of blood banks be kept in the

hands of those who have it now and of this association.

Medicine did not grow up to the magnificent cooperative effort it is now by the work of social planners and bureaucratic directives. It is the work of physicians, striving together for the common good. The needs are not too big for such cooperation. Jefferson said "Government governs best which governs least."

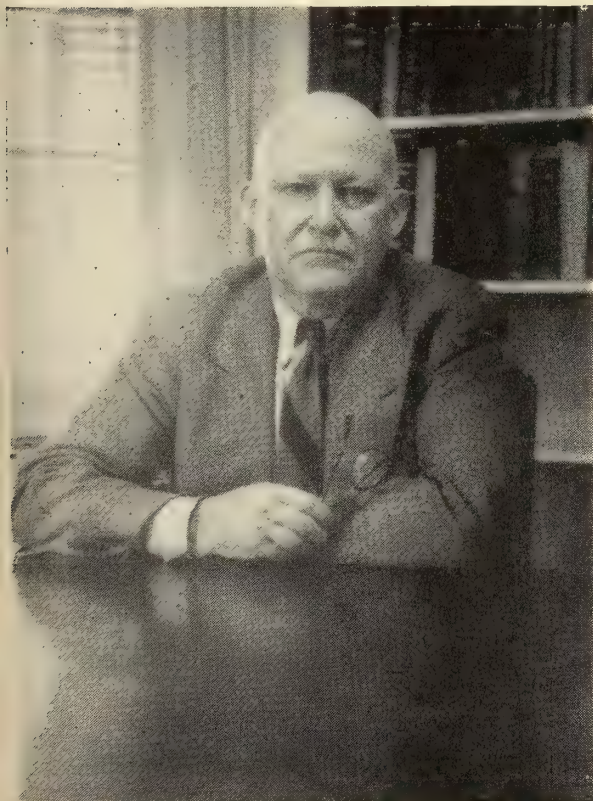
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## ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

***An informed profession should be a wise one.***

### PRESIDENT ANDERSON



The President of the Louisiana State Medical Society, Dr. Gilbert C. Anderson, completes his term of office in April, 1948. As a marker along the long road of service he has travelled for organized medicine, we

take pleasure in presenting a brief biographical sketch.

Dr. Anderson was born in Jackson, Tennessee, educated in the public schools and graduated by Southwestern Baptist University, of that city, with the degree of Bachelor of Arts. Doctor of Medicine was granted by the College of Physicians and Surgeons of Columbia University and he served as intern in the City Hospital and House Surgeon in the New York Hospital, both of New York City.

During the first World War he entered the United States Army as first lieutenant and was immediately assigned to neurological surgery at which he worked at Camp Greenleaf and General Hospitals Nos. 11 and 41.

Soon after discharge two very important and far reaching factors influenced his life; the first his marriage to Mildred Hodges Moore of Norfolk, Va. and the second an intensive postgraduate course in neurological surgery as a Fellow at the Mayo Foundation during the last year of which he was first assistant to Drs. Adson and Craig. For work done during and in connection with this Fellowship he was awarded the degree of Master of Science (in Surgery) by the University of Minnesota.

Upon completing his fellowship he came to New Orleans and entered the practice of

his specialty late in 1927. He was appointed on the Faculty of Tulane University which post he held until the founding of the Medical Center of Louisiana State University where he accepted the appointment which he now holds. Very soon after his arrival in New Orleans he aligned himself with organized medicine and has been active in that field of endeavor until the present time, filling various posts from time to time including the Presidency of Orleans Parish Medical Society. He is on the staff of several hospitals in New Orleans, is a member of local, sectional and national societies and a diplomate of the American Board of Neurological Surgery.

Following discharge from the U. S. Army after the first World War he accepted a commission in the Federalized Guard of the State of New York and was assigned to the 71st. Infantry Regiment; upon moving to Minnesota he joined the Organized Reserve and was very active in that work until the outbreak of the second World War which found him a Lieutenant Colonel and acting Colonel in command of the 312th. Medical Regiment, and Division Surgeon of the 84th Division, Organized Reserve; he reported for active duty and was discharged for physical reasons but worked during the war for Selective Service as a Member of Medical Reference Board. He also served as Lieutenant and Captain in the Civil Air Patrol and as Lieutenant Colonel and Chief Medical Officer of the Louisiana State Guard.

His hobby is his camp at Grand Isle.

The past year the administration of the affairs of the State Society has been a difficult task. Problems involving vital interests of the Society have been numerous. The ever-increasing battle against political medicine has had to be fought. The program of promoting solidarity in our ranks and of improving our public relations has been effectively supported. The Society is fortunate in having enjoyed the good effects of its president in so critical a year.

When Dr. Anderson relinquishes the presidency of the Society, it is not felt that he is retiring from an active part in the

affairs of organized medicine but that he is merely joining the distinguished group of past presidents whom the Society has been proud to honor and upon whom it depends so heavily for advice, help and material service.

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## ANNUAL MEETING

We wish to call your attention to the approaching meeting of our State Society in Monroe, April 12, 13, and 14th; headquarters in the Frances Hotel. Those who have not yet secured reservations should at once contact Dr. J. W. Cummins, who is chairman of the Hotel and Meeting Rooms Committee. The Annual Meeting this year will be most representative, and we are sure, one of the largest ever held. It will include an impressive scientific program and this should be an excellent time to review the scientific progress of medicine and surgery. It will also afford an opportunity to meet many distinguished colleagues. Many of the speakers are men of national and international reputation who have demonstrated marked proficiency in the respective subjects assigned to them. The following is the synopsis of the meeting:

### Monday, April 12

Morning and afternoon: Meeting of House of Delegates; noon: Luncheon for House of Delegates; evening: General Public Meeting. This will probably be held at the Neville High School Auditorium and the speakers of the evening will be Dr. Morris Fishbein, of Chicago, and Dr. James E. Ayre, of Montreal. The meeting will be an open forum on the subject of Cancer.

### Tuesday, April 13

Morning and afternoon: Scientific Program; noon: Luncheon for Members; evening: President's Reception.

### Wednesday, April 14

Morning and afternoon: Scientific Program; noon: Specialty Luncheons.

Your attention is particularly called to the out-of-state speakers. Dr. Ira T. Nathanson of Boston, Mass.; Dr. Harry S. N. Greene, New Haven, Conn.; Dr. J. E. Faber, Rochester, Minn.; Dr. F. R. Lock, Winston-Salem, N. C.; Dr. Wm. F. Guer-



riero, Dallas, Texas; Dr. W. Ambrose McGee, Richmond, Va.; Dr. Herbert Mantz, Kansas City, Mo.; Dr. Jos. M. Hayman, Jr., Cleveland, Ohio; Dr. George B. Eusterman, Rochester, Minn., and Dr. James E. Ayre, Montreal.

It is expected that serious thought and attention will be given to this splendid scientific program that has been arranged. The doctors of the Ouachita Parish Medical Society and their friends in Monroe are doing everything in their power to make your visit in this city a pleasure, and a profitable program and suitable entertainment is being provided for everyone.

Following are copies of communications received from the Mayor of Monroe and the Secretary of the Chamber of Commerce, which are evidence of your welcome to the City of Monroe.

February 14, 1948

Dr. P. T. Talbot  
New Orleans, Louisiana  
Dear Dr. Talbot:

It is my understanding that the Louisiana State Medical Society Annual Convention is to be held in Monroe, Louisiana, April 12-14, 1948.

Monroe is a beautiful city and our people are known for their hospitality. We are indeed proud that your organization chose to have the convention here and we will do all we can to make it a success.

Please feel free to call on us if there is any assistance we can render.

Yours very truly,

H. H. BENOIT, *Mayor*.

February 13, 1948

Dr. W. L. Bendel  
Wright-Bendel Clinic  
Monroe, Louisiana  
Dear Dr. Bendel:

We are delighted to learn that the Louisiana State Medical Society is to hold its Annual Meeting in Monroe, beginning April 12. You may rest assured that your colleagues in the medical profession and their wives will receive a very warm welcome from the citizens of Monroe.

If this organization can assist you in any way in making arrangements for your convention, we wish you to feel free to call on us. We extend to the Medical Society our best wishes for a most successful convention.

Sincerely yours,

H. G. BAILEY, JR., *Manager*,  
*Chamber of Commerce*.

The tentative program of the Woman's

Auxiliary which will provide wonderful entertainment for all the visiting ladies will be found in the Woman's Auxiliary section of this issue.

The following is a list of the committees and chairmen:

General Chairman: John G. Snelling.

Advisory Committee: Dr. John G. Snelling; Dr. A. Scott Hamilton; Dr. C. P. Gray, Sr.; Dr. J. Q. Graves; Dr. George W. Wright, and Dr. DeWitt T. Milam.

Badges: Dr. F. P. Rizzo advises that appropriate badges will be furnished at the Registration Desk.

Banquet: Dr. A. V. Miller, Jr. is in charge of all banquet arrangements.

Commercial Exhibits: Dr. Clifford Johnson reports that he is receiving the contracts from commercial exhibitors and will allocate the proper space and will do all in his power to assist in the exhibits.

Entertainments: Dr. C. B. Flinn is active in completing all necessary entertainment for our visitors.

Budget and Finance: Dr. Henson Coon will make disbursements as required and is receiving checks daily.

Golf: Dr. Fred Marx will stage a tournament, the time to be announced later and suitable prizes awarded. Bring your clubs and other paraphernalia.

Hotel and Meeting Rooms: Dr. J. W. Cummins suggests that you make reservations as early as possible and will select halls and rooms at headquarters for the various programs.

Lanterns and Projectors, Sound Equipment: Dr. M. W. Hunter has both a slide machine and motion picture machine in readiness, and will arrange for an operator.

Program: Dr. Glen Gallaspy has charge of the program and will endeavor to see that it is carried on at proper time.

Registration: Dr. P. L. Perot will see that the registration desk is in a conspicuous place on the Cherokee Terrace.

Luncheons: Dr. B. J. Lecour promises to have enough for everybody to eat.

Scientific Exhibits: Dr. J. E. McConnell promises suitable space for all exhibits.

Transportation: Dr. George Varina will

arrange for cars for the golfers and any others who request them. Please submit requests at the registration desk.

Barbecue: Dr. D. T. Milam and Dr. Hen-son Coon will see that everyone is well taken care of at the barbecue.

Decorations: Will be taken care of by the Ladies Auxiliary Committee—"nuff said."

Please write or telephone these chairmen if they can be of any service to you.

WILLIAM L. BENDEL, M. D., *Chairman,*  
*Publicity Committee.*

WELCOME TO THE TWIN CITIES  
AND OUACHITA PARISH

Monroe and West Monroe, the Twin Cities of Northeast Louisiana are interest- ing and traditionally southern cities situ- ated on opposite banks of the Ouachita River. These beautiful cities vividly con- trast the old romantic south with the latest in modern community development. Homes, churches, schools, and business houses re- flect the architecture of our times. Monroe and West Monore are constantly engaged in joint efforts to make this a better com- munity in which to live.

Monroe's growth is the phenomenal story of a rural village shedding its swaddling clothes over night and growing into a mod- ern metropolitan city within a decade with an estimated population in 1946 of 33,000.

West Monroe, which began to grow rath-

er rapidly following the developments of gas fields had an estimated population of 12,000 in 1946.

The Twin Cities, 45,000 strong, are a staunch pillar in the economic, commercial, educational, religious, political, and social structure of Louisiana.

Selman Field operated during the war as a bombardier and navigation training cen- ter, is now leased to the City of Monroe as a municipal airport.

The Twin Cities are located on transcon- tinental highway 80 and five other high- ways radiate from these cities.

The five largest hotels have a total of about 800 rooms.

Northeast Jr. College of the Louisiana State University, located in the outskirts of the beautiful Sherrouse Addition, ranks as one of the leading institutions of the state.

Natural gas development began in 1916, grew in the next quarter century to the point where the "Monroe Gas Field" was the largest in the world.

Monroe and West Monroe have a commis- sion council form of government. Monroe owns its public utilities and transportation facilities. The city is heated with natural gas. The Mayor of Monroe is H. H. Benoit; H. G. Bailey, Jr., Secretary of Chamber of Commerce. William Rodriguez and Ruffin Tidwell are Commissioners. In West Mon- roe, the Mayor is C. C. Bell.

LOUISIANA STATE MEDICAL SOCIETY NEWS  
C A L E N D A R

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

THE COUNCIL ON MEDICAL SERVICE AND  
PUBLIC RELATIONS NOW HAS THREE  
WEEKLY RADIO PROGRAMS

The Council on Medical Service and Public Rela- tions now has three radio programs on an active

basis. The programs are broadcast weekly and the radio stations use the AMA transcribed series and present them in cooperation with the Council on Medical Service and Public Relations of the Louisiana State Medical Society and the local par-



ish medical society.

The two new stations added to the broadcast schedule are KTBS, Shreveport, and KWCJ, Natchitoches. "The Story of Surgery" is being presented every Saturday at 4:00 p. m. over KTBS in Shreveport, and "Keeping Your Baby Well" may be heard over KWCJ in Natchitoches every Monday at 3:30 p. m. KNOE in Monroe, the first station to present our series, is broadcasting the program "What to Do Before the Doctor Comes," every Wednesday at 1:30 p. m.

All of the series are of a 13-week duration and when completed will be followed by other series.

Doctors in the listening areas should encourage their patients to listen to the broadcasts.

#### AMERICAN ACADEMY OF GENERAL PRACTICE OF LOUISIANA

Since this organization was formed last July, it has made unusual progress. The national organization lists about 3,300 members, with 45 states and one territory represented. Four states have organized on a state level, and many more contemplate organization in the near future. Kansas City will become the permanent home of the national organization next month. An executive secretary, Mr. Mac Cahal, probably the most capable person in his field, has been employed and is now gradually taking over the active management of the national organization. Plans for a journal are expected to be made within a year. Louisiana has been a leader in the movement from the beginning. Not only was this the first state to organize on a state level, but also all the congressional districts are organized on a district level. This will be the first state to hold a scientific meeting which will be held at the Bentley Hotel in Alexandria on April 3-4. Every doctor is cordially invited to attend. Watch your newspaper for further news about the meeting.

#### THIRD ANNUAL NATIONAL CONFERENCE ON RURAL HEALTH

Dr. F. S. Crockett and his committee on rural medical service of the A. M. A. presented one of the most interesting meetings held on this subject, at the Palmer House on February 6-7. The theme of the program this year was CHILD WELFARE.

About three hundred were present from all over the United States and represented outstanding medical men and laymen interested in rural health. Louisiana had ten representatives including eight doctors, Mrs. T. R. Tomlinson, chairman of the rural health council of Louisiana and Mr. Frank Lais, Jr., executive secretary of our Council on Medical Service and Public Relations. The general medical field was represented by both specialists and general practitioners.

The following items were almost completely agreed on by everyone present.

1. Rural areas are not as healthy as the urban centers.

2. Rural people, though obtaining the best medical care that they have ever had, still have poor medical care as compared to those in the city.

3. There is a definite need all over the country for better equipped hospitals in rural areas.

4. Rural areas need more and better trained general practitioners, dentists, and other allied professional help.

5. Many rural areas are badly in need of well located and well operated health centers.

6. Teachers in our educational system should be more health conscious and should have some extra training in health.

7. Better medical care is dependent upon improved economic standards in many localities. This is particularly true in the poorer districts.

8. Regular and complete physical and dental examinations should be a "must" in rural areas particularly among the school children. Many states are requiring that school children be examined every three or four years.

Probably the most fascinating part of the program was a symposium entitled "Rural Youth Looks at Health" given by four youngsters, representing the Grange, the Farm Bureau, the Farmers Union and the Cooperative Milk Producers Federation. One had just finished high school, two were still in college and one is a rural school teacher; all are probably still in their teens. They opened our eyes in many respects because we were surprised at their knowledge of conditions of rural health. They are demanding better rural health and they expect and will get better rural health.

The following four problems confront the farmer today according to their presentation.

1. Nutrition.

2. Poor health and poor educational facilities.

3. Few or no health units. Poor or no hospital facilities in the community.

4. The vanishing general practitioner.

In discussing nutrition they stated that the nutrition of the farmer was poor for two reasons. First, that he had not been educated to the fact of what is good nutrition and, second, that many times he sells off his best foods in order to improve his economic condition.

Poor health and education are caused by a number of situations; the poor economic condition of the farmer in many cases, the general tendency of everyone to ignore the farmer in preparing for good health and the indifference of the farmer himself many times to health problems. They stated that the lack of education and poor health go hand in hand.

While cities and urban centers have been very alert in putting in health units and good hospitals, rural areas have been very backward in carrying out these problems. It was brought out that this is as much the farmers' fault as it is the doctors'

but if we do not solve them, the politicians will ultimately take over. Only one of the four representatives advocated compulsory health insurance; the other three definitely recommended voluntary prepayment medical and hospital insurance as one of the answers to their problems.

Then they took a particularly hard swing at the general practitioner. They stated that the specialist had taken over but indicated that what the rural people need more than anything else to give them good medical care is a well trained general practitioner.

They are working on the above problems and expect to solve them.

Health education was stressed as an important factor in all school health programs. It was stressed that the teachers themselves should be better trained in health. The school lunch program in most cases should be enlarged and expanded to take care of all, but community cooperation is important to put these projects through.

Rural public health organizations such as our Rural Health Council in Louisiana is an important factor in looking after needs of the people in rural areas. The role of the Parent-Teachers Association, the health units and dental care was stressed. Woman's Auxiliary organizations can be called in many times to assist in putting through these public health programs.

Dr. Hoge from the Surgeon General's office of the United States Public Health Service stressed the importance of the Hill-Burton Bill to construct rural hospitals. With one-third of the total expense put up by the Federal Government and one-third by the state (if that is done) this leaves only one-third of the total construction to be borne by the community and makes it possible for many communities to have a well organized hospital which otherwise they would not be able to afford.

Dr. R. V. Platou, of Tulane, gave a remarkable paper on the pediatric service being carried out under the auspices of the State Board of Health and L. S. U. and Tulane Medical Schools. He stressed the role of the general practitioner in connection with health of children in rural areas.

Summarizing, it is realized as never before that rural young people want and are going to have good medical care. They are willing to work for this and expect our help and cooperation. Dr. Crockett and his committee, the rural medical services of the various states and the farm people, through their own organizations, are all working cooperatively to give good medical care. None of these wants state or socialized medicine.

#### NEWS ITEM

Dr. L. Roland Young, formerly of Covington, Louisiana, is now practicing in Daytona Beach, Florida and recently received an appointment as member of the Consulting Staff of the Lake County Medical Center in Eustis, Florida. Dr. Young also

recently addressed the Volusia County Society of the International Child Educational Association on "Mental or Psychological Prophylaxis in the Primary Grade Child" at the Lenox Avenue School, Daytona Beach.

#### EXPANSION OF A. M. A. SPEAKERS' PROJECT

The Board of Trustees of the A. M. A. has assigned a new duty to the Bureau of Health Education.

The bureau hereafter will endeavor to make more speaking engagements for traveling members of the A. M. A. headquarters staff.

The idea behind this assignment is that when a speaker travels a considerable distance from Chicago to attend a meeting or make an address, his time in the distant community will be used to the greatest possible extent. Most communities are eager for speakers from A. M. A. headquarters, and the Bureau of Health Education has been instructed by the Trustees to procure from all headquarters offices the names and speaking qualifications of traveling representatives from the A. M. A. The Bureau will then endeavor to arrange additional engagements in the community to which the speaker is going or in nearby communities.

The Bureau of Health Education desires particularly to have Women's Auxiliaries to local medical societies register their needs for speakers.

These requests will be coordinated with the availability of traveling members of the A. M. A. headquarters staff whenever possible, so as to furnish local communities with the service of these traveling representatives.

The Bureau will also be glad to hear from the secretaries of state and county medical societies the names of available speakers in their jurisdictions so that requests for speakers received at headquarters can be referred to local speakers, either direct or, if preferred, through the secretaries of state and county medical societies.

This experimental service, if successful, can be the nucleus for the nationwide Speakers' Bureau which, in coordination with local speakers' bureau organizations within the structure of the A. M. A., can render an important service to the public through the medical profession.

#### THE LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

The Annual Meeting of the Louisiana-Mississippi Ophthalmological and Otolaryngological Society will be held at the St. Charles Hotel in New Orleans on Saturday, April 17.

#### Program

8:30 a.m.	Registration
9:00	Call to Order
	Preliminary Announcements



## Appointment of Committees

President's Address: Dr. Noel T. Simmonds, Alexandria, La.

Secretional Obstruction and Bulbar Poliomyelitis, Dr. Thos. C. Galloway, Evanston, Ill.

The Preparation of Patients for Intraocular Surgery, Dr. Walter Stevenson, Quincy, Ill.

12:30 p.m. Luncheon

Executive Session

2:00

The Management of Complications of Ocular Surgery, Dr. Watson Gailey, Bloomington, Ill.

The J. Raymond Hume Memorial Address—Vertigo: Differential Diagnosis and Treatment, Dr. J. R. Lindsay, Chicago, Ill.

5:30

Cocktail Party for Fellows, guests and their ladies

The Registration Fee of \$10.00 includes the luncheon and the cocktail party.

#### AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC.

The general oral and pathology examinations (Part II) for all candidates will be conducted in Washington, D. C., by the American Board of Obstetrics and Gynecology from Sunday, May 16, through Saturday, May 22, 1948. The Shoreham Hotel in Washington will be the headquarters. Formal notice of the exact time of each candidate's examination will be sent him several weeks in advance of the examination dates. Hotel reservations may be made by writing direct to the Shoreham Hotel.

Candidates in military service are requested to keep the Secretary's Office informed of any change in address.

Applications are now being and will be received until November 1, 1948 for the 1949 examinations. For further information and application blanks address Paul Titus, M. D., Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

#### AMERICAN SOCIETY FOR THE STUDY OF STERILITY

The Fourth Annual National Session of the American Society for the Study of Sterility will be held in Chicago at the Congress Hotel, on June 21-22. The two-day program will be divided into a special series of panel discussions on male infertility, with papers to be read on female and miscellaneous infertility aspects, on the second day. Additional information concerning this meeting may be obtained from the Secretary, Dr. John O. Haman, 490 Post Street, San Francisco 2, California.

#### JOHN TOLSON O'FERRALL, JR.

1885-1948

Dr. John Tolson O'Ferrall, Jr., Councilor of the Second Congressional District, died in New Orleans on January 31, 1948. Dr. O'Ferrall, a graduate of Tulane University Medical School in 1908, was an active and interested member of organized medicine for many years. He served on many committees of the State Society and was Councilor of the Second Congressional District from 1943 until his death.

#### JOSEPH ALPHONSE O'HARA

1869-1948

Dr. Joseph Alphonse O'Hara, of New Orleans, died on February 25. Dr. O'Hara was president of the Louisiana State Medical Society 1938-39 and actively interested in the affairs of the organization at all times. He was a graduate of the 1900 Class of Medicine of Tulane University.

#### WOMAN'S AUXILIARY

At a meeting of the Ouachita Parish Auxiliary in January Mr. Frank Lais, Jr. spoke on Louisiana Physicians Service, Inc. and activities of the Council on Medical Service Public Relations of the State Society. Radio programs sponsored by the Louisiana State Medical Society and the Woman's Auxiliary of Ouachita Parish will be presented through the cooperation of KNOE as a public service feature. The topics of the first series of programs will be "What to Do Until the Doctor Comes". Mrs. H. V. Collins will serve as general chairman of a committee whose object will be to present the aims and ideas of the Louisiana Physicians Service to the public. Mrs. C. B. Flinn is radio chairman, Mrs. Hayden Cutler, public relations chairman and Mrs. J. W. McConnell and Mrs. C. P. Gray, Jr., will head the speakers' bureau.

Plans were discussed for the State Convention to be held in Monroe and capable Mrs. De Witt Milam was appointed chairman.

Here is the list of activities that are of importance to the Auxiliary.

Monday, April 12

12:00 noon—Luncheon honoring state and parish officers at the La Casa Tea Room, \$1.25.

4-6 p. m.—Tea honoring Mrs. Warren, Mrs. Owens, Mrs. Anderson and the wives of the guest speakers, to be held at the home of Dr. and Mrs. A. G. McHenry, 1810 Riverside.

Tuesday, April 13

12:30 p. m.—Barbecue, Bernstein Park.

8:00 p. m.—Banquet and Dinner Dance, Hotel Frances.

Wednesday, April 14

12:30 p. m.—Style Show and Luncheon, Virginia Hotel, \$2.00.

## BOOK REVIEWS

*Diseases of Metabolism*: Edited by Garfield G. Duncan, M. D. 2d ed. Philadelphia, W. B. Saunders Company, 1947. Illus. Pp. 1045. Price, \$12.00.

The second edition of this excellent book, completely revised and presented in a new slenderer format (though the text has actually been somewhat expanded) will be heartily welcomed by student, general practitioner, and internist alike.

The five years between the appearance of this edition and its distinguished predecessor have seen many significant advances in the field of metabolic diseases, and in no other text are these advances presented as conveniently and accessibly as here. In addition to the familiar chapters on carbohydrate, protein, lipid, mineral, water, and vitamin metabolism, all completely revised new chapters on thyroid and kidney disease have been added.

Dr. Duncan and his authoritative co-authors have produced a book which no internist or well-informed general practitioner can afford to be without.

J. R. SNAVELY, M. D.

*Textbook of Human Physiology*: By William F. Hamilton, Ph. D. Philadelphia, F. A. Davis Company, 1947. Pp. 504. Price \$6.00.

Teachers of physiology to medical students have long felt the need of a smaller textbook in keeping with the length of time devoted to the formal teaching of this subject in the first or second year curriculum. Dr. Hamilton has attempted to supply this need by preparing a textbook in which the material is presented dogmatically and restricted to the things that the average student can encompass in the short time he is in the Department of Physiology. Thus the entire complex field is presented in about 480 pages.

For the most part, Dr. Hamilton has succeeded quite well in his difficult objective. The various sections on the nervous system, respiration, blood, circulation, digestion, fluid exchange, metabolism and the endocrines are well organized, adequately illustrated and the material clearly presented. By way of minor criticism, the question may be raised as to whether some of the material on methods of measurements of circulatory pulses, etc. might not have been abbreviated and the space given to some other topic, such as the endocrine system. This system is treated in 33 pages although the author in his introductory chapter emphasizes that "disturbances in endocrine function form an important chapter in modern medicine." The textbook will be chiefly valuable to the first year student who supplements his reading with the information obtained from lectures and who will go to the more detailed

texts for special and additional information when necessary.

H. S. MAYERSON, PH. D.

*The Physico-Chemical Mechanism of Nerve Activity*: By David Nachmansohn, et al. Annals of the New York Academy of Sciences, XLVII, Art. 4, 1946. Pp. 375-602.

This monograph embodies the lectures given at a conference held under the auspices of the New York Academy of Sciences in which the leading investigators in the field participated. The lectures covered the most recent experiments in the field of nerve activity, synaptic transmission, and nerve metabolism. There are twelve lectures on various aspects of these fields, an introduction by Tracy J. Putnam, and a conclusion by John F. Fulton. Much of the work reported is concerned with the question as to whether the transmission of nerve impulses is electrically or chemically mediated. The electrical hypothesis is upheld by Dr. Eccles, whereas, Nachmansohn has given in detail his reasons for believing in the chemical mediation theory. Of particular interest is the lecture by Dr. Gerard entitled "A Critique of the Role of Acetylcholine," in which he questions the importance of acetylcholine in junctional transmission in the central nervous system and suggests that the time is ripe for a new concept of nerve impulse transmission.

The monograph is recommended to those who are interested in obtaining a first hand report of the modern concept of nerve activity as given by the workers who are best equipped to present this information.

H. S. MAYERSON, PH. D.

## PUBLICATIONS RECEIVED

Butterworth & Co. (Publishers), Ltd., London, England and C. V. Mosby Company, St. Louis: British Surgical Practice (8 Volumes, Volume 1), edited by Sir Ernest Rock Carling, F. R. C. S., F. R. C. P. and J. Paterson Ross, M. S., F. R. C. S.

C. V. Mosby Company, St. Louis: Occupational Medicine and Industrial Hygiene, by Rutherford T. Johnstone, A. B., M. D.; Hernia (3rd edition), by Leigh F. Watson, M. D., F. I. C. S.

W. B. Saunders Company, Philadelphia: Treatment in General Practice (6th edition), by Harry Beckman, M. D.

Williams & Wilkins Company, Baltimore; Skeletal Tuberculosis, by Vincente Sanchis-Olmos, M. D.

The following publications were incorrectly listed in the January, 1948 issue:

Lea & Febiger, Philadelphia: The Foot and Ankle (3rd edition), by Philip Lewin, M. D., F. A. C. S.; A Primer of Cardiology, by George E. Burch, M. D., F. A. C. P. and Paul Reaser, M. D., Surgical Disorders of the Chest (2nd edition), by J. K. Donaldson, B. S., M. D., F. A. C. S.



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### PRURITIS ANI AND VULVAE\*

M. T. VAN STUDDIFORD, M. D.

AND

L. D. McLEAN, M. D.

NEW ORLEANS

Pruritis ani or vulvae, or of both, is a common condition and a problem of general interest to physicians, since these patients consult not only their general practitioner, but the gynecologist, the proctologist, the urologist, the internist, the surgeon and the dermatologist.

The literature is somewhat confusing and one gets the impression that there is rather general disagreement as to etiology and treatment, with different authors championing different etiological factors as the most common cause.

#### SYMPTOMATOLOGY AND MORPHOLOGY

The itching occurs in an embarrassing location and because of this the patient often hesitates to seek the aid of his doctor and in the meantime applies local medication suggested by advertisements, friends, or the druggist. This, not uncommonly, finally results in such an intensification of the pruritis from primary irritation or dermatitis venenata, that he is forced at last into the doctor's office for an examination. In the chronic and intractable cases, the pruritis becomes so much of a problem that it dominates the patient's personality and affects the course of his life as well as the lives of those with whom he lives.

The itching is worse at night and keeps

the patient awake, creating a state of nervous exhaustion approaching hysteria. We have even seen the development of true hysteria, with the patient lifting her pelvis high off the bed in the presence of family and friends, screaming out in uncontrolled anguish, and scratching the parts until they were almost completely denuded.

A factor that complicates some cases and makes them more difficult to handle is that sometimes an erotic pleasure is produced by scratching or rubbing the inflamed vulva or anus. On rare occasions a patient will confide that he or she gets a sensation similar to sexual intercourse from the experience, but more commonly, the idea will be suggested by the way in which the patient describes the paroxysms of itching.

Although patients with pruritis ani and vulvae may complain with equal eloquence, they do not always present the same morphologic picture in the involved areas. Some patients show little, if any, evidence of skin disturbance, while most show varying degrees of lichenification, thickening, maceration and excoriation. On first examination the areas often show acute inflammation from the effects of irritating topical applications. The difference in the amount of lichenification and thickening that is found has been explained<sup>1</sup> by the fact that the constitutionally hypersensitive or atopic individual responds to repeated scratching or rubbing by the formation of edema, lichenification and thickening, while the person without this background does not respond to repeated trauma with the same pattern; instead the skin remains apparently normal.

The age incidence usually includes the

\*Read before the Sixty-seventh Annual Meeting of the Louisiana State Medical Society, New Orleans, May 14, 1947.

group between 30 to 70 with the highest incidence between 45 and 65. The disease has usually been present for a year or more and sometimes it is of 15 to 20 years' duration.

#### CLASSIFICATION AND ETIOLOGY

According to textbooks and much of the current literature, pruritis ani and vulvae should be classified into two groups: first, primary or idiopathic cases for which no cause can be found; second, secondary pruritis ani and vulvae in which some etiologic factor can be found. The following list is included just to tabulate the various conditions which have been reported to be associated etiologically with pruritis ani and vulvae.

##### A. *Local rectal*

1. Hemorrhoids
2. Fissures
3. Fistula
4. Cryptitis and papillitis with streptococcic invasion and possible sensitization
5. Rectal constipation
6. Uncleanliness
7. Proctitis

##### B. *Local vulvar*

1. Leukorrhea from any cause (especially trichomonas)
2. Vulvitis and vaginitis
3. Uncleanliness

##### C. *Parasitic*

1. Pin worms in children
2. Trichomonas
3. Monilia
4. Epidermophyton
5. Scabies
6. Pediculi

##### D. *Chemical*

1. Alkaline or acid urine
2. Alkaline or acid feces
3. Skatol in the feces
4. Calcium or oxylate crystals in the urine.
5. Self or prescribed medication

##### E. *Traumatic*

1. Tight fitting girdles or underwear
2. Rough toilet tissue
3. Friction and moisture in obesity
4. Strong soaps and hot water in bathing

##### F. *Pelvic conditions*

1. Tumors producing congestion of the area, including pregnancy and malignancy
2. Prostatitis

##### G. *General metabolic*

1. Thyroid dysfunction
2. Diabetes
3. Kidney disease
4. Anemia
5. Liver disease particularly with jaundice
6. Hodgkin's disease and leukemia
7. Degenerative changes in skin and mucosa associated with the climacteric and later, senile changes including leukoplakia and kraurosis.

##### H. *Allergic*

1. Dermatitis venenata
  - a. Local medication for pruritis, hemorrhoids, or leukorrhea.
  - b. Nail polish and other substances accidentally carried by the hands
2. Sensitivity to drugs as phenolphthalein, opium, oral ivy extract
3. Sensitization to foods
4. Sensitization to bacterial toxins

##### I. *Psychogenic*

1. Psychoneurosis with substitution phenomenon
2. Hysteria
3. Masturbation

Most of the conditions in the above list can produce anal or vulvar itching but when the cause is usually obvious, as in the case of pediculosis or trichomonas, treatment of the cause brings prompt relief. In those persons with chronic intractable pruritis ani or vulvae, however, we seldom find a local or systemic disease that satisfactorily explains the condition.

The importance of rectal pathology is often stressed, but such eminent proctologists as L. A. Buie<sup>2</sup> and L. G. Bodkin<sup>3</sup> say that seldom, if ever, do they recognize local rectal pathology as being an actual causative factor. Bodkin states that in "95 per cent of cases seen by the proctologist, no observable lesion or disease can be demonstrated." Buie states that the "in-



stances in which an anal sinus, a hemorrhoid, an ulcer, a fissure, a stricture, or something of that kind, can be found are rare." Further evidence against these factors as being entirely responsible for intractable pruritis is the fact that when such local conditions are found and are removed surgically, the pruritis is either not benefited or at the best is only temporarily relieved.

Probably the next most frequently cited cause for pruritis ani and vulvae is the fungi, either a species of the epidermophyton or *Monilia albicans*. If the fungi are so frequently the cause, and we believe the mycologists who tell us that no disease should be classified as being caused by a fungus without at least demonstrating the fungus, either by scrapings or by culture, then we wonder why some scientifically minded individual has not settled the matter by publishing a sizable series of cases with cultural proof. The answer to this is the fact that the demonstration of a pathogenic fungus is very difficult in these cases. Although most of the patients we see have been treated for a mycotic infection with various fungicidal preparations, including gentian violet, Whitfield ointment and carbolfuchsin paint, the evidence for fungus infection is rather flimsy. The diagnosis is apparently made because the area involved is usually circular, superficial mycotic infection of the inguinal region and buttocks is rather common, and the most prominent symptom of dermatomycosis is itching. Furthermore, everyone expects fungi to grow in a moist intertrigenous area. Intractable pruritis ani or vulvae is rarely seen in association with typical tinea of the inguinal region or buttocks and the cases we see have not been helped by fungicides.

While it is perfectly true that pruritis is a symptom and not a disease in itself, a thorough physical examination is frequently completed without a satisfactory explanation for the intense itching that occurs in these cases.

There are certain factors, however, that characterize the patients we see. In the first place, these individuals possess the

same type of personality. They are hard-working, overactive and restless, with more plans than they can accomplish. They do their own and other people's work and drive themselves mercilessly. At the same time they worry over trifles and have a tendency to be emotionally unstable. They all have symptoms of nervous exhaustion. These patients do not know how to relax. They do well while occupied with their tasks during the day but at night they are restless and mentally active. After a short period of physical inactivity, the edema that has been maintained during the day begins to subside and it is then that the pruritis becomes their major problem. After a night spent with only snatches of sleep they are tired and exhausted, but feel better later in the day when they again become active. These people live on nervous energy and the vicious cycle is perpetuated. It is like a squirrel in a cage trying to catch his tail: exhaustion is the result.

In the second place there is usually some precipitating problem which the individual cannot satisfactorily solve or adjust, such as financial worries or family troubles. The joke about the cause of a man's pruritis ani being traced to the stack of unpaid bills hidden under the seat of his easy chair, and cured by a legacy from his rich old uncle, might not be so far wrong in some cases.

When this precipitating factor or seemingly insurmountable problem occurs in an individual with the previously mentioned constitutional background, there is usually the development of a substitutive mechanism. Some organ or system of the body is selected and it acts as the shock organ for the personality as a whole. Such individuals may develop any one of a long list of functional diseases, including conditions of the cardiovascular system, gastrointestinal system, and so on.

The third factor of importance is the selection of the anus or the vulva as the shock area. This is accomplished most probably by some irritation in the area which focuses the attention of the personality there. This localizing irritation that makes

the individual conscious of the anus or vulva may be due to any of the factors previously tabulated. We would like to emphasize several conditions which seem to act as the trigger mechanism in some cases. During the climacteric, in women particularly but also in men, the skin and mucous membranes not only begin the degenerative changes seen to culminate in senility but the skin is more sensitive to mechanical irritation.<sup>5</sup> Most patients would fall into this age group. Hemorrhoids and fissures are common ailments and frequently associated with a mild pruritis. A purulent discharge from trichomonas or any other cause is usually associated with some pruritis. Emphasis should be laid upon the drugs used in the treatment of leukorrhea with caution against strong irritating chemicals and drugs with a high index of sensitivity. We have also known cases of intractable pruritis ani that began with the surgical removal of hemorrhoids, probably due to sensitivity of the patient to the accompanying antiseptic applications. We believe that not infrequently the primary irritation is due to tight fitting girdles or underclothes. Patients are sometimes seen with pruritis ani or vulvae who also have itching of the ear canals and eyelids. Some of these cases have proved to be due to sensitivity to nail polish.

Kraurosis and leukoplakia are conditions which must be recognized and distinguished from the lichenification and maceration of pruritis ani and vulvae. Leukoplakia does not differ in its appearance on the mucous membrane of the vulva or anus from that occurring in the mouth. Kraurosis is associated with marked atrophy and atresia of the orifice. These conditions are malignant or develop malignancy in approximately 20 per cent of cases.

#### TREATMENT

It is often a very difficult problem to gain the confidence of a patient with pruritis ani and vulvae and to insure cooperation in carrying out a schedule of treatment. They greet you with the statement that they have a drug store on their cabinet shelves and that they have tried every

known ingredient suggested by friends, druggists, and doctors, without success. They want and demand radical measures, which probably accounts for the extensive surgery of nerve cutting, sloughing alcohol injections and tattooing procedures that are all too frequently performed. Suffice it to say, that a high percentage of recurrences occur after these procedures and we do not recommend their use.

One of the most important things to remember is that the itch cannot be controlled by counterirritants or strong medication. One cannot burn the itch out because the medication acts in the same way that scratching does and the vicious cycle is simply perpetuated.

The procedure we use in the treatment of these cases is simple. We try to give the patient some insight into the cause for his or her itching. Any of the factors that might have acted as the trigger mechanism are dealt with accordingly. We recommend the use of loose-fitting underwear. For men the loose-fitting one-piece garment is excellent, whereas tight shorts and jockey strap shorts are particularly bad. The most satisfactory way to relieve a paroxysm of itching and at the same time soothe the inflamed skin is by means of wet compresses. We use a solution of boric acid and corn starch at room temperature, and advise the maintenance of the pack in position much in the same way that a sanitary napkin is worn. These packs should be worn even during sleep while the condition is severe. Compresses are essential when the area shows evidence of acute irritation by local medication as often the tissues will not even tolerate plain petrolatum. The parts are kept clean by applying a zinc oxide ointment containing benzocaine directly before bowel movements and gently sponging the area afterward with moistened soft toilet tissue or absorbent cotton. A suppository containing benzocaine is inserted twice a day and if there is an area of maceration and dermatitis around the anus or there is involvement of the vulva, then the zinc oxide ointment is applied more often. The benzocaine acts effectively only on the



mucous membrane and the muco-cutaneous junction. The hands should be restrained during sleep. The patient is instructed to get up early and not to take naps during the day, to avoid "turning the clock."

Small doses of phenobarbital taken during the day and one hour before bedtime usually do a great deal to help this type of person relax. We find that many women, even though they have ceased menstruating several years previously, still have symptoms of the menopausal syndrome and estrogenic substances are indispensable in the treatment of their condition. The estrogens not only serve to modify the nervous tension, but also have a physiological effect upon the skin and mucosa of the area involved.

X-rays have come in for some unjust criticism in the treatment of pruritis ani and vulvae because their use has been abused. When used intelligently, however, they can be of unquestionable aid. It must be remembered that x-rays will not cure the patient. The beneficial effect is attained by anesthetizing the nerve endings in the area, which relieves the pruritis long enough to interrupt the vicious cycle of itch, scratch, dermatitis, itch, and so on, and allow the skin to regain its normal state. Large doses are unnecessary and 75 to 100 r should be sufficient. Usually four or five weekly treatments give the necessary time interval and no more radiation is given. If the pruritis is not relieved, then there is failure in one of the other aspects of treatment and further radiation would not be of any benefit.

#### CONCLUSION

In conclusion, we want to emphasize that in spite of the fact that in the majority of cases no organic lesion is found either locally or systemically that entirely explains the pruritis ani and vulvae, none the less a careful examination should be made.

Most cases seem to present this combination of circumstances: some irritation to the area focuses the attention of the personality on the vulva or anus; this occurs in an individual who has a constitutional background of nervous instability and who at

this particular time has some serious worry or problem. The anus or vulva thus becomes the outlet or shock organ and a vicious cycle is set up. It must be borne in mind that there are two cycles instead of one as commonly recognized. First, the local skin cycle of itch, scratch, dermatitis, itch, and secondly, the vicious cycle of overactivity, worry, nervous exhaustion, or emotional instability. Both of these cycles must be understood and dealt with in obtaining results in the treatment of pruritis ani and vulvae.

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### THE PRESENT STATUS OF OUR KNOWLEDGE CONCERNING THE SPREAD OF POLIOMYELITIS\*

DAVID E. LOVEMAN, M. D.

NEW ORLEANS

#### INTRODUCTION

Besides having a personal interest in poliomyelitis, I selected this topic in order to try to bring together and evaluate much experimental data that have been performed in somewhat of a haphazard fashion. One must admit at the beginning that there is still little or no direct data upon which to build a picture of how the virus enters the human body, from what sites it invades the central nervous system, and in what peripheral site

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it multiplies or is liberated. I used the word "virus" in the above statement, yet we cannot be certain that poliomyelitis actually is a viral disease; it may be proved later to be a deficiency disease or a disease that belongs in a category hitherto undescribed. Furthermore, at present, the human being is the only known reservoir of the virus, and the monkey, the only known experimental animal. Finally, it is necessary to theorize from a few facts, to correlate these theories with clinical experience and then to draw conclusions which are at best only shrewd guesses.

In this paper I shall present experimental data which deals with the transmission of poliomyelitis and attempt to correlate these experiments with what has been observed clinically. Conclusions will be drawn and finally, postulations will be presented which I believe deserve serious thought and experimentation in the near future.

#### PROPERTIES OF THE VIRUS

That the etiology of poliomyelitis is viral in nature must be accepted as a working hypothesis at present. While not definitely proved that the agent is a virus, it behaves in a manner similar to members of the virus group, in that it cannot be seen with the microscope; that it lives intracellularly and depends on living cells for growth and that it is highly specific, being a strictly neurotropic agent. With the aid of the newly developed electron microscope, it is estimated that its size is approximately 10  $\mu$  to 12  $\mu$ , one of the smallest viruses known.

That the poliomyelitis virus is an especially hardy one, is shown by its remarkable resistance to physical and chemical agents. It withstands drying *in vacuo* for at least a month and exposure to 50 per cent glycerine for several years. Phenol, ether, acetate, gastric and intestinal juices, bile and icebox temperatures do not destroy the virus, while copper sulfate, mercurochrome, mercury bichloride, potassium hydroxide, potassium permanganate in concentrations of 0.1 per cent and 50 degrees C. (30 minute) heat do inactivate the agent.<sup>1</sup> Filtration and chlorination, in a concentration

usually employed in water purification, are ineffective in removing the virus.<sup>2</sup>

Of all the viruses known to attack the human nervous system, the virus of poliomyelitis has the most limited of host range. The virus isolated from human tissue has been found to be pathogenic only for certain monkeys and chimpanzees and not for mice, guinea pigs or rabbits. Many investigators have attempted to adapt strains of the virus to the rat or guinea pig, but for the most part these experiments have not been successful, and the conclusions drawn from such experiments are of doubtful value when applied to the human form of the disease. The poliomyelitis virus exhibits strict neuronotropism and will not multiply in the undifferentiated embryonic chick or mouse tissues.

There are many immunologically distinct types of the poliomyelitis virus and the antibodies developed against one type will not protect against another, so that secondary attacks due to a heterogenous strain are possible. Finally, the virus seems to consist entirely of protein, or of protein in combination with nucleic acid.<sup>3</sup>

#### PORTALS OF ENTRY

Most of the conclusions concerning the method by which the virus gains access to the human body have been drawn from experimental work done on the rhesus monkey, animals which actually are not susceptible to the disease. Many times these conclusions have not been correlated with clinical experience and simple logic; therefore, much chaos has arisen concerning the evaluation of these data. However, these animals are the only ones available in numbers to perform the experiments upon and we must make the most of an obviously handicapping factor in the experimentation of poliomyelitis.

The human portal of entry concerns us for many reasons, but particularly if it gives a clue as to what carries the virus. Is the virus associated in nature with a drop-let of nose spray; with contaminated food or other objects; or with a contaminated biting insect? In order to view the experiments concerning each of these possibilities with a critical eye, we may begin with what



is known concerning the sites of predilection and the selective sites of location of the virus in the human body. The most extensive work on this has been done by Sabin and Ward.<sup>4</sup> Their work is most illuminating on this subject because it deals with human tissues affected with poliomyelitis and not that of monkeys. They set out to determine: (a) whether or not a certain system was affected; (b) what might be the centrifugal or centripetal pathways pursued by the virus outside the central nervous system, and (c) whether or not at the time of death the virus is distributed indiscriminately throughout the central nervous system. Their material was derived from necropsies of six or more human cases of poliomyelitis, under aseptic conditions and an individual handling of each tissue or group of tissues to be tested. The tissues were ground up, centrifuged and extracted with ether and were then inoculated intracerebrally into rhesus monkeys. If the monkey developed flaccid paralysis, experimental poliomyelitis was diagnosed. The monkeys either died or were killed and the detection of typical lesions by pathologic means was determined; finally, passage of the virus from these monkeys to a second series of monkeys was performed. Their results on the distribution of the virus in the tissues of fatal cases of poliomyelitis are as follows:

(a). The absence of demonstrable virus in the olfactory bulbs and anterior perforated substance indicates that the olfactory pathway need not be affected in human beings.

(b). The absence of virus in the nasal mucosa suggests that it is not the site of virus multiplication and dissemination.

(c). The absence of virus in the salivary glands indicates that the saliva is not a likely means for its elimination.

(d). The positive results with the tonsils and pharyngeal mucosa, are probably due to the pharyngeal tissue rather than the tonsils.

(e). Next to the central nervous system the virus is distributed predominantly in the alimentary tract and is present not only

in the contents but also in the washed walls of the various parts of the tract including the pharynx, ileum, and occasionally the colon.

(f). Infection of the walls of the alimentary tract appears to be the result neither of the generalized dissemination of the virus nor of secondary centrifugal spread, but rather that of primary localization or *portal of entry*.

(g). The distribution of virus in the central nervous system is limited to certain areas and is not as indiscriminately disseminated as viruses which can invade through the blood vessels (equine encephalomyelitis), or those which having entered by a specific nervous pathway, are capable of extensive centrifugal spread (rabies).

(h). In the absence of evidence of any appreciable centrifugal spread to peripheral collections of nerve cells, the demonstration of virus in the abdominal sympathetic ganglia of one case is significant in suggesting one of the possible routes of virus progression in certain instances.

Thus it can be concluded that the virus is distributed predominantly in two systems: (1) certain regions of the nervous system and (2) the alimentary tract.

With the sites of location of the poliomyelitis virus in the human body in mind, we may now proceed to consideration of the vast amount of data concerned with the experimental portals of entry of the agent. Most of this work has centered around infecting rhesus monkeys by three routes: (1) the olfactory portion of the nasal mucosa; (2) the mucosa of the digestive tract, (3) subcutaneous and intracutaneous inoculation.

To begin with it might be well to state the conception of Toomey<sup>5</sup> concerning the obligate affinity of the poliomyelitis virus for grey fibers of the nervous system. He postulates that the only way the virus can be absorbed in the human being is by grey end fibers of somatic or autonomic nerves, and once absorbed from these sites it spreads along the axis cylinders toward the central nervous system and causes damage only when it reaches the nerve cell. In

other words, it is only when the virus comes into contact with these fibers it can be absorbed and thus spread to the vital nerve cell. That this is true is well demonstrated in experiments and in nature. The poliomyelitis virus must be widely disseminated in nature, yet everyone does not contract the disease, due possibly to many factors, but one in particular, that is, that the virus does not come into contact with grey fibers of those who remain well. In the laboratory, monkeys have been exposed to the virus under similar conditions, yet not in any report have all the animals displayed the clinical and pathologic picture of poliomyelitis, thus in some the grey fibers must not have been exposed to the agent. That the grey fibers are the ones affected is shown by the fact that they are the only ones usually affected in the disease. From this conclusion, one can see that the portal of entry may be any of the three mentioned above, provided that the grey fibers of that tissue come into contact with and absorb the virus.

#### THE OLFACTORY PORTION OF THE NASAL MUCOSA

The observations of earlier workers seemed to point to the fact that the poliomyelitis virus spreads in nature by means of contact of a susceptible person with an infected one. It was surmised that this was accomplished by means of infected droplets of nose spray. This led to much experimental work with monkeys, which were inoculated with the washings of the nasopharynx of known cases of poliomyelitis. Usually these reports showed that from one-half to three-quarters of the animals developed poliomyelitis; this was considered proof that the virus was present in the nasopharynx and lent support that the virus of poliomyelitis was spread by human contact.<sup>6</sup> Other experiments were performed in which the virus was instilled intranasally in monkeys. The animals were found to be easily infected by this method and necropsy studies on them showed inflammatory infiltration along the olfactory pathway. If, however, this pathway were surgically interrupted or the nasal mucosa were treated with certain chemicals, infection could not

be produced. These data presented a strong argument that the virus was spread from one person to another by the nasopharynx of one becoming infected with droplets of nose spray from the other. Lending support to this argument was the anatomically known fact that the olfactory mucosa is the region where the nerve endings are nakedly exposed to the exterior, and the region where the virus could realize immediate contact with nerve cells,<sup>7</sup> so that until the past few years it was widely held that the common natural portal of entry of the virus was the olfactory portion of the nasal mucosa. It was said to spread from this area in the nose along the olfactory nerve to the olfactory bulbs and from there along the olfactory tracts to the central nervous system.

#### THE MUCOSA OF THE DIGESTIVE TRACT

In 1934, experimenters began to question the olfactory route as the most natural portal of entry, because only rarely could it be demonstrated that the olfactory bulbs of human cases showed a trail of inflammation. This adds weight to the previous statement that what has been proved experimentally cannot always be correlated with clinical and pathologic evidence in human cases of poliomyelitis.

Since 1934 investigators have become cognizant of the fact that poliomyelitis is essentially a disease of the temperate zone, occurring during the summer months and that its epidemiology closely resembles that of diseases whose known portal of entry is the alimentary tract. This stimulated workers to investigate the digestive route as a more likely portal of entry of the virus of poliomyelitis. In earlier experiments monkeys were fed the virus by stomach tube and no attempt was made to absolutely rule out the virus contaminating the olfactory mucosa by vomiting, so that only the recent experiments will be considered in which this route is definitely known not to have been contaminated.

Faber and Silverberg<sup>8</sup> reported infecting a monkey by applying the virus covered with digestible fat capsules in the esophagus. The olfactory route was blocked by applying zinc sulfate to the nasal mucosa,



and was not contaminated as shown later by no inflammatory lesions demonstrable in the olfactory mucosa.

Howe, Bodian et al.<sup>9</sup> have shown that active virus is present in the human oropharynx by using nasal swabs rubbed against the posterior wall of the oropharynx of humans with poliomyelitis as their means of obtaining the agent instead of nasal or pharyngeal washings. This material was inoculated intracerebrally into monkeys, 50 per cent of which developed poliomyelitis.

Many investigators, including Sabin<sup>14</sup> and Ward,<sup>15</sup> Paul and Trask,<sup>16</sup> Flexner, have all produced poliomyelitis in cynomolgus monkeys by simple feeding, as placing the virus in bananas, dropping suspension of the virus in the mouth, and so on. These experiments were non-traumatic, involving no injury to the mucous membranes and are thus comparable with natural infection. Faber, in an attempt to determine whether the upper or lower portion of the alimentary tract was the portal of entry, came to the conclusion that the upper portion (mouth, pharynx, esophagus) was more vulnerable for poliomyelitis.<sup>10</sup>

In reviewing these experiments, Toomey<sup>11</sup> states that we should not be too astonished at those cases of poliomyelitis which develop following tonsillectomy or tooth extraction, because under these circumstances the virus and frayed edges of peripheral nerves can meet, as a result of which disease follows. He points out that the gastrointestinal tract, actually an external organ yet contained within the body, is not as protected as the skin, for example, in not having any external layer or "epimucosa" to prevent absorption. In fact, absorption should occur any place along the intestinal tract, and the poliomyelitis virus is no exception. He indicates that in the more naturally occurring disease, perhaps there is a small denuded area with exposed nerves at some point in the alimentary tract, which acts as the portal of entry of the virus. The agent is thought to travel via the abdominal sympathetic nerves and ganglia from the gastrointestinal tract to the central nervous system.

#### SUBCUTANEOUS AND INTRACUTANEOUS INOCULATION

That poliomyelitis can occur after inoculation of the virus into the skin has been shown on several occasions, the most striking of which occurred in a laboratory worker. The virus was accidentally inoculated subcutaneously in this worker, following which she developed the disease. Strimpert and Kessel<sup>12</sup> injected intradermally several monkeys with the virus and obtained "takes" in some. They concluded that this was an inconsistent way of producing poliomyelitis. While definitely shown that the disease can be produced in this manner, it is obviously a very unnatural portal of entry in the usual case of poliomyelitis.

In summing up, it appears that the alimentary tract is the primary site of attack by the virus in most naturally occurring cases. While not denying that other routes are possible, it seems more logical to conclude that the digestive tract is the system usually implicated in the portal of entry of poliomyelitis, as sustained by the facts presented above: that it is a site of predilection of the virus in the human body, that experimental disease can be produced by simple feeding of the infectious agent to monkeys, that the virus can usually be isolated from stools of clinical cases of poliomyelitis, and that the epidemiologic statistics of poliomyelitis tie it in with the diseases whose known portal of entry is the gastrointestinal tract. It might be mentioned that some workers have postulated that infection may occur by the respiratory tract.<sup>13</sup> However, when one considers the clinical picture and what is known concerning the sites of location of the virus in the human, there is very little or no support of this concept.<sup>14</sup>

#### PORTALS OF ELIMINATION

From what has been said concerning the portal of entry, the portals of elimination become obvious. The virus has been demonstrated by inoculation of nasopharyngeal washings, tonsillar washings and stools into monkeys. These inoculums were usually obtained from other monkeys that

showed clinical signs of the disease, with the exception of the stool inoculum. In practically every case of poliomyelitis, human or experimental, the virus can be easily demonstrated in the stools, while it is very difficult to detect in nasopharyngeal washings. This lends support to the argument that the nose and mouth are not common portals of elimination of virus and that virus in the stool does not represent secretion from the nose and mouth that have been swallowed and concentrated in the intestinal tract.<sup>15, 16, 17</sup>

The virus may be found not only in the stools of paralytic patients, but also in those of patients with non-paralytic and abortive types of poliomyelitis, and even in apparently healthy individuals. Thus the question arises, do chronic carriers of poliomyelitis exist? Horstmann and Ward<sup>18</sup> have shown that there is a progressive decline during the first eight weeks of the disease, in the number of convalescent patients excreting virus. After the twelfth week the virus could not be found in the stools of the patients. Thus it seems that chronic carriers do not exist.

The virus has never been demonstrated in the urine from the bladders of poliomyelitis patients.<sup>19</sup>

Incidentally, it may be mentioned here that the virus is not absorbed by the blood stream from the nasal or alimentary mucosa; also transfusion from a paralyzed monkey to a well animal does not result in disease of the recipient monkey.<sup>20</sup>

#### SOURCES OF INFECTION AND POSSIBLE VECTORS

As to the reservoirs of the poliomyelitis virus in nature, only speculations can be presented which are based on a few known facts. The known facts can be stated rather briefly. Paul and Trask,<sup>21</sup> have demonstrated the presence of virus in sewage from several large cities. The virus, however, has never been demonstrated in "running tap water." As to vectors, the non-biting filth flies have been found to harbor the virus. It is interesting to note, however, that they harbor the agent within their bodies, and not so much on the exterior. To

demonstrate this, flies were trapped in: (1) areas where there was a potential source of the virus in the form of exposed excreted human feces; (2) in areas where no such source was apparent, that is, in some of our cleanest and most sanitary urban areas. Part of the flies caught were ground up, extracted with ether and then inoculated into monkeys, others were only washed and that material inoculated into monkeys. For the most part positive "takes" came from the ground up suspension. It is known that flies produce a "vomit spot" before feeding and it may be surmised that they can serve as carriers of the virus by their contamination of food with these vomit spots.

In reviewing the literature, poliomyelitis virus has never been demonstrated in the mosquito, stools of sick dogs, well water, paralyzed chicken or in the tomato plant.<sup>22</sup>

#### SEASONAL INCIDENCE

Poliomyelitis is a year round disease. Epidemics continue into the cold weather and cases are reported even in the severest winters. It is true, however, that epidemics usually occur in the late summer and it has been shown how the disease progresses through the country as warm weather occurs in various sections. From these observations, we can draw only limited conclusions; they are that the winter cases may be due to contact spread, whereas the sharp seasonal peak in summer and fall may be due to insects disseminating the virus (the insects contaminating themselves from infected human feces).

#### SUMMARY

In this paper I have tried to bring together much experimental data concerning the spread of poliomyelitis. Properties of the virus, portals of entry and exit, sources of infection, possible vectors and seasonal incidence were considered. To sum up, it appears that the virus of poliomyelitis is a strictly neurotropic agent, and that it is an especially hardy one. It has been detected in urban sewage, filth flies, nasopharyngeal washings and stools of patients with the disease. The virus of poliomyeli-



tis has been found to be pathogenic only for humans, monkeys and chimpanzees, thus it has a limited host range. Experiments on the portal of entry of the agent were presented and it seems that the most likely natural site is the alimentary tract, the virus being absorbed and traveling along the grey fibers of the sympathetic nervous system to the central nervous system, where it attacks the nerve cells. That other routes are possible, for example, olfactory tract, respiratory tract, and subcutaneous inoculation, is not denied, but considered unlikely when correlated with clinical and pathological evidence. At present the only known reservoirs of the poliomyelitis virus in nature are stools from paralytic and abortive cases and urban sewage. That flies may carry the virus and disseminate it during epidemics is presented as a possible explanation of the sharp seasonal peak of poliomyelitis (actually a year round disease) in the summer and early fall.

#### CONCLUSIONS

Conclusions drawn from this study concerning the spread of poliomyelitis are as follows:

1. That poliomyelitis is spread in many ways, the most common one being the ingestion of the virus on food, fingers; and so on, which were previously contaminated by flies or by coming in contact with a known case of the disease. Other means of spread are: (a) susceptible persons coming into contact with infected persons, who contaminate the susceptibles with infected droplets of nose spray; (b) the subcutaneous inoculation of the virus.

2. Some epidemics of poliomyelitis may be due to infected milk or water but these outbreaks would fall into the previously mentioned category of ingestion of the virus.

3. Much more work will have to be done before any conclusions concerning the spread of poliomyelitis can be drawn. The above conclusions are for the most part speculations and are not based on concrete

experimental data, but on circumstantial evidence only.

4. It is my belief that poliomyelitis is possibly spread by the mosquito. Work on this possible vector has for the most part been avoided due to the fact that the virus has only rarely been demonstrated in the blood stream of patients with poliomyelitis, thus the conclusion that the mosquito has no way of becoming infected. Despite this fact, I believe that after more experimentation has been done, the mosquito will be incriminated as the vector of poliomyelitis.

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# UROLOGICAL COMPLICATION FOLLOWING OPERATION FOR IMPERFORATE ANUS

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AND

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NEW ORLEANS

Recently a case of recto-urethral fistula in a male infant who had had surgical correction of an imperforate anus, came to our attention. The problems arising in the management of this unusual complication prompted us to make this report.

In the available literature, very little warning is sounded as to the danger of urethral injury in the surgical correction of imperforate anus.

Congenital anomalies of the anus and rectum are said by different authors to occur in from one in fifteen hundred to one in five thousand new-borns. In approximately 50 per cent of these anomalies, which vary from rectal stricture to an absence of the lower bowel, there is an associated fistula either to the bladder, urethra, vagina, or perineum. We have reviewed the cases of imperforate anus at the Charity Hospital for the past five years. Fourteen such cases comprise this series, one of which we are here reporting because of an urological complication.

Of the fourteen cases, four had either recto-urethral or recto-vesical fistula present at birth; four had urethral injuries inflicted at the time of surgical correction of imperforate anus with resulting recto-urethral fistula.

## EMBRYOLOGY

A brief review of the embryology of the lower urinary tract and lower bowel will enable one to understand better the development of these anomalies. According to Patten,<sup>1</sup> at approximately five weeks of fetal life, the allantois has already been formed from an evagination of the hind

gut. The gut just caudal to the origin of the allantois becomes enlarged to form the cloaca. The hind gut at this time still ends blindly, being covered by a thin ectodermal depression under the root of the tail. This depression is called the proctodaeum and the covering termed the cloacal membrane. Normally, the membrane eventually ruptures, establishing the caudal outlet of the gut.

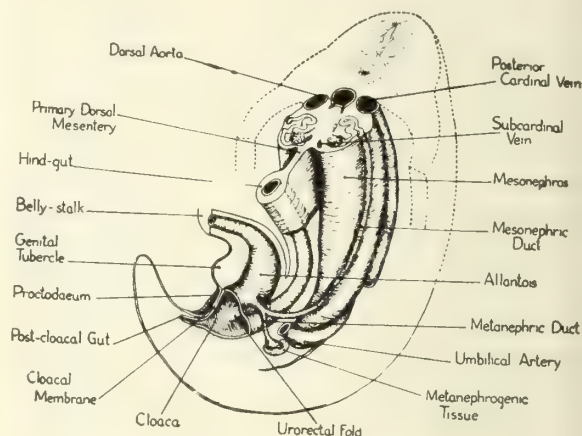


Fig. 1. Schematic ventrolateral view of urogenital system of human embryo between 4 and 6 mm. (fifth week), showing the cloaca before it is divided into the rectum and the urogenital sinus. (Redrawn from Kelly and Burman: "Diseases of the Kidneys, Ureters and Bladder," Fig. 55, courtesy, D. Appleton-Century Co.)

Before this opening is established important changes are taking place internally. The cloaca begins to be divided into a dorsal part, which forms the rectum, and a ventral part known as the urogenital sinus. This division is effected by the growth of the urorectal fold, a crescentic fold, the two limbs of which bulge into the lumen of the cloaca from either side from above downward. As the fold cuts progressively deeper into the cloaca, a wedge-shaped mass of mesenchyme follows into the epithelial fold, thus forming a robust septum between the urogenital sinus and the rectum. The separation of the cloaca is complete before the cloaca membrane ruptures and the two parts, the urogenital sinus and the rectum, open independently. The opening of the rectum is the anus and the opening of the urogenital sinus is the ostium urogenitale.

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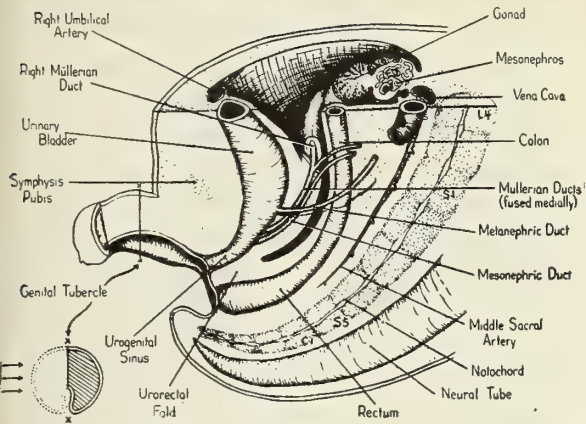


Fig. 2. Semischematic drawing of reconstruction of the urogenital system of a human embryo of eighth week, showing the cloaca completely divided into the urogenital sinus and the rectum by the urorectal fold. (Patton's New Human Embryology, courtesy The Blakiston Co.)

Failure of the proper development of the urorectal fold or failure of the cloacal membrane to rupture may result in the deformity of the rectum, bladder, urethra, or vagina. The resulting deformity may be a bifid bladder, imperforate anus, rectovesical fistula, recto-urethral fistula, recto-vaginal fistula, rectoperineal fistula, and possibly a combination of the above conditions.

#### CASE REPORT

Math Smith, colored male, eighteen months of age. Admitted to Charity Hospital 10/29/46 because of failure to pass his urine through the urethra since operation for imperforate anus eighteen months previously.

**PAST HISTORY:** Patient admitted to Charity Hospital 8/11/45 when two days old, with a diagnosis of imperforate anus. Physical examination at that time revealed, in addition to imperforate anus, marked abdominal distention and temperature of 102 degrees Fahrenheit. According to the mother's statement, the baby was seen to void normally and an urinalysis was negative. An x-ray of the abdomen and pelvic region was made with the patient in the inverted position, and the gas bubble in the rectum was reported to be approximately 1 cm. from the anal dimple. On 8/13/45, two days after admission, the patient was operated on for correction of imperforate anus. Following operation, the mother stated that the patient did not void per urethrum. Patient was discharged on 9/25/45, the 44th hospital day.

Patient readmitted 10/9/45, when two months of age, at which time he was still passing all the urine through the rectum. Examination revealed

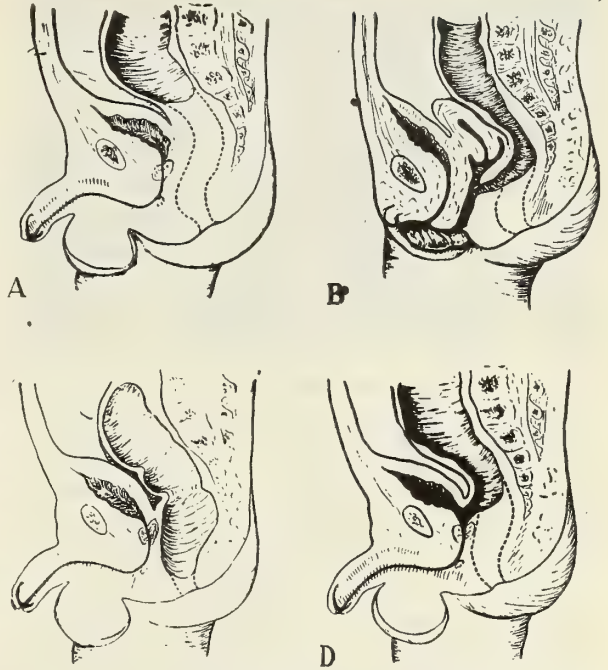


Fig. 3. Anomalies due to disturbances in the development of the cloacal region. (Redrawn from Corning.) A. Anal atresia combined with obliteration of lower part of rectum. B. Aanal atresia combined with a rectovaginal fistula. C. Uncomplicated anal atresia. D. Anal atresia combined with rectovesical fistula. ("Abdominal Surgery of Infancy & Childhood", W. B. Saunders 1941, courtesy Ladd & Gross.

the urethra completely obstructed in the bulbo-membranous area. Treatment was deferred until the child was older.

**PRESENT ADMISSION:** The patient's urinary status was the same as on previous admission. His growth and general health were excellent. The urological survey consisted of an urethrogram, which revealed an obstruction in the bulbo-membranous region, and an intravenous pyelogram which failed to outline the upper urinary tract satisfactorily, but showed a partially filled, normal appearing bladder.

On 12/13/46, a suprapubic cystotomy was done revealing a normal bladder. Passage of any type of filiform or sound from below was impossible. Retrograde passage of the sound resulted in prompt entrance of the sound into the rectum through the posterior urethra. In employing sounds from above and below in an attempt to approximate the ends of the sounds, it was found that the retrograde sound did not have sufficient curvature to meet the sound from below. With the substitution of an uterine sound from above, the curve of which was increased sufficiently, it was possible to approximate the ends of the two sounds and to re-establish the continuity of the urethral canal.

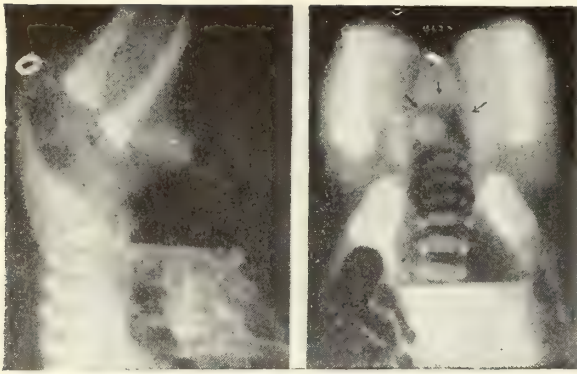


Fig. 4. Roentgenograms of child with imperforate anus to show position of the rectal pouch (outlined with arrows) in relationship to anus (marked with an oval piece of lead.) The child is inverted, so that gas will rise and indicate caudal extent of the rectal pouch. (Fig. 114 "Abdominal Surgery of Infancy & Childhood", W. B. Saunders 1947, courtesy Ladd & Gross.)

Following this, the urethra was dilated up to a #18 French, after which a #10 French catheter was passed with ease. A Pezzer catheter was left in the suprapubic wound and the indwelling urethral catheter was tied in.

The urethral catheter was removed at the end of the third week, and on clamping the suprapubic tube, the patient voided satisfactorily. The suprapubic tube was then removed and the suprapubic fistula promptly healed. The patient was seen again one month later, at which time a #13 sound was passed with ease and the patient was voiding grossly clear urine without difficulty.

#### COMMENT

Although very little attention has been directed to the likelihood of urethral injury during surgical correction of imperforate anus, in this series of fourteen cases this mishap occurred four times. This is an incidence of a little less than 29 per cent. It appears timely now to warn of the danger of this complication and offer any known preventive measures.

Ladd and Gross<sup>2</sup> recommend dissection of the rectum in the sacral curve rather than anteriorly, to avoid injury to the urinary structures. These authors also advocate an indwelling urethral catheter during the operation so that the urethra may be palpated and injury avoided. If this does not make identification of the urethra satisfactory, it occurs to us that an urethral sound or a

solid flexible bougie held in place by an assistant would make palpation of the urethra in the wound an easy matter.

To know the caudal extent of the rectal pouch and to know of the existence of any associated urinary fistula is a pre-operative requisite. In 1930 Wangenstein and Rice<sup>3</sup> described an ingenious method to determine the extent of the blind rectal pouch. It consists of making a roentgenogram of the abdomen and pelvis with the infant in the inverted position. The gas in the colon rises and outlines the distal end of the rectal pouch, making it possible to estimate the distance between the anal dimple and the caudal end of the rectum.

When the dissection has to be carried higher up, urethral injuries certainly would seem to be more likely than when nothing more than the cloacal membrane has to be incised.

A recto-urethral or rectovesical fistula associated with imperforate anus should present no diagnostic difficulty. The presence of meconium in the urine or passage of gas per urethrum would establish the diagnosis. Furthermore, lateral cystourethrogram should also be made when this condition is suspected.

In the case reported, operative injury of the urethra with a resulting urethrorrectal fistula undoubtedly occurred. There was nothing in the operative notes to indicate that urethral injury was suspected by the surgeon who corrected the imperforate anus.

The operation performed is an old procedure used for dilating impassable urethral strictures. The use of a malleable uterine sound, curved to meet the requirements, was prompted by the inability to introduce a rigid sound into the urethra from above.

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# CENTRAL FRACTURES OF THE NECK OF THE FEMUR\*

A CRITICAL REVIEW OF 300 CASES\*\*

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Every orthopedic surgeon treating "acute," or fresh, fractures of the neck of the femur by internal fixation has been asked by the patient, or relatives one, or possibly all, of the following questions:

(1) What is the chance of surviving the operation at my age?

(2) What chance do I have of the bones "knitting"?

(3) What are my chances of walking again?

(4) Will the hip be painful when I am able to walk?

In addition to these questions, which are of prime importance to the patient, many surgeons, without access to a large series of cases, or without the time to conduct a survey, are interested in mortality rates, unions and non-unions, aseptic necrosis, and arthritic changes of the head of the femur.

A study has been made of 300 cases of central fracture of the neck of the femur treated by internal fixation in which Smith-Petersen nails were used in 285 cases, and Knowles pins in 15 cases. These cases are unselected, and go back to 1930 at which time the first hip was nailed in the clinic. All the cases were considered fresh fractures and were nailed within a period of three weeks following fracture. Many have been nailed of greater duration than three weeks, but have been excluded as it is the general impression that they do not fall into the category of fresh fractures.

Fractures of the base of the neck, and through and between the trochanters are not included in this study as they are extracapsular, and do not present the same difficulties of non-union, aseptic necrosis and degenerative changes of the femoral head

that is characteristic of fractures through the central portion of the neck of the femur. The fractures to be considered are intracapsular, and in 1935 Friedrich Pauwels classified them into three groups based upon the plane of fracture through the neck and the corresponding shearing strain. He draws a line horizontally through the anterior superior iliac spines and measures the angle formed by this, and a line drawn through the plane of the fracture. Those cases in which the angle is less than 30 degrees are classified as Type I. Since some orthopedists consider these as abduction fractures and in a relatively horizontal plane, many of which appear roentgenologically to be impacted, and feel that they will heal without operation, they have been excluded from this study.

The angle is from 30 to 50 degrees in Pauwels' Type II fracture, and there is a corresponding increase in shearing strain which necessitates internal fixation of the fracture. In Type III fractures, the angle is from 50 to 90 degrees, and as the angle approaches a right angle, the shearing strain increases in proportion. Only Pauwels' Type II and III fractures are included in the study.

In the group of 300 cases, there were 252 Type II fractures, or 84 per cent, and 48 Type III fractures, or 16 per cent. These 300 fractures occurred in 294 patients, but in none of the six bilateral cases were both hips injured simultaneously.

## AGE DISTRIBUTION AND SEX OF PATIENTS

Central fracture of the neck of the femur is an affliction chiefly occurring in females in later life.

TABLE I  
AGE DISTRIBUTION

	Cases	Total Per cent
Under 40 years	15	5
40-59 years	50	16
	92	(30.6%)
60 and over :	87	(29%)
	56	(18.7%)
	<hr/> 300	<hr/> 100

TABLE II  
SEX DISTRIBUTION

	Cases	Total Per cent
Female	246	82
Male	54	18
	300	100

\*Read before the Sixty-seventh Annual Meeting of the Louisiana State Medical Society, New Orleans, May 14, 1947.

\*\*From the records of Willis C. Campbell Clinic, Memphis, Tenn.

There is such a striking difference between the incidence of the two sexes that there must be definite reasons. It is the impression that elderly men lead a more active life than elderly women, consequently, there is not as much osteoporosis of the bones. The preponderance of women may also possibly be due to their wider pelvis, with a resulting genu valgus.

#### MORTALITY

All patients, relatives, and the surgeon are interested in the first question that presents itself at the time of operation and postoperatively; namely, the survival of the patient.

There were 28 deaths in the first six months following the 300 operations, 21 of which occurred within the first four weeks. An all over mortality of 9.3 per cent appears approximately correct, and an interesting finding in the study was that, of the 65 cases under 60 years of age, there was not a single death. In the decade from 60-69 years, the mortality was 5.4 per cent, from 70-79, 10.3 per cent, and from 80-96 years, the mortality climbed to 25 per cent.

The most common cause of death was pneumonia, and this has apparently been reduced in the later years by internal fixation and getting patients up within a few days to 24 hours, postoperatively. Other causes of death were listed as myocardial failure, coronary occlusion, coronary thrombosis, hypertensive cardiovascular disease, and postoperative infection.

#### FOLLOW-UP OF CASES

The follow-up of cases of fracture of the neck of the femur has been rather disappointing, probably because of the patients' advanced age, in many cases poor general health, transportation difficulties during the war and, no doubt, many just refused to take the time to return for checkups. The younger groups of patients seemed to return very well, but as age increased, the follow-up declined. As the study progressed, it became increasingly evident that no case with less than one year's follow-up with adequate clinical and roentgenologic data should be included in the statistics of unions, non-unions, aseptic necrosis and

arthritic changes of the head. In the younger patients, definite bony union is often seen in the roentgenograms within less than a year. In the greater number of cases, however, it is a mistake to try to determine the presence of union under one year, for occasionally bony union occurs after a year, especially where there is an appreciable absorption of the neck. Of the 300 cases reviewed, only 47 per cent of 141 had adequate follow-up for over one year.

#### UNIONS AND NON-UNIONS

This is the second important question regarding a fractured neck of the femur in which the principals, including patient, relatives and the surgeon, are interested.

Based on the 141 cases mentioned above, it was found that as a whole, bony union occurred in 86.5 per cent (122 hips) and non-union in 13.5 per cent (19 hips) of the hips. The highest percentage (93.3 per cent) of unions was in 45 cases under 60 years of age, with actually no non-unions in 11 cases under 40 years. In the 96 cases over 60 years of age the percentage of union was 83.3.

There are evidently several factors influencing union of these fractures. The above statistics indicate that bones with senile changes do not unite as readily as younger bones. Some authors have felt that the great shearing strain exerted on the Type III fractures renders them more prone to non-union. In this review, however, the percentage of non-unions was 10.3 per cent (three in 29) in Type III fractures and 14 per cent (16 in 112) in Type II fractures.

The Clinic staff has long had the impression that accurate reduction and proper nailing of the fragments influences union. That there is a certain foundation for this impression is shown by the fact that 69 per cent of the unions had good or excellent reductions and nailings, while there was union in 31 per cent in which the reduction and nailing was either only fair or poor. In the non-unions, ten of the nineteen were attributed to poor reductions, inadequate mechanical fixation and premature removal of the nail. The remaining nine fractures followed satisfactory reductions and nail-



ings, but two were in patients with Paget's disease involving the head and neck of the femur. From this, it is concluded that proper alignment and nailing of the fragments must play some part in union, but there may be other factors that enter into the healing process, not the least of which may be the interruption of the blood supply to the head and cervical fragment.

#### ASEPTIC NECROSIS

The head and neck of the femur receives its blood supply from the inferior gluteal, obturator and circumflex arteries, mostly through the posterior capsule, and with a small branch, apparently of relative unimportance, through the ligamentum teres.

Injury to the capsule in which the blood vessels are torn or thrombosed at the time of fracture or nailing, may result in aseptic or avascular necrosis of the head. In the group of 122 unions, there were 41 cases which showed aseptic necrosis at some time during the follow-up, this constituting 33 per cent of the group. While the age of the patient seems to have some influence on union of these fractures, there does not seem to be any relationship between age and aseptic necrosis. Of the 11 patients under 40 years of age, three of them showed aseptic necrosis. A check was made of the series of x-rays of the patients showing aseptic necrosis to determine the time of appearance of the changes in the head, and it was found that it was discernible in 19 cases at 9-15 months, in an additional 11 cases in 15-27 months, and in 11 cases after 27 months. From this, it seems that the greatest number of cases begin to show changes in the head at about one year, and that the lapse of time up to about two and a half years, at least, gives no assurance that aseptic necrosis will not develop. In the non-unions, approximately 60 per cent of the cases showed aseptic necrosis of the femoral head.

Absorption of the neck sufficient to be roentgenologically evident occurred in 11 per cent of the unions resulting in partial extrusion of the nail and delaying union.

#### ARTHRITIC CHANGES IN THE HEAD

The answer to the third question, "will

I be able to walk?" can theoretically be answered by saying that all those getting union should be able to walk. However, this is not actually the case, and along with the fourth question, "Will the hip be painful?" they should be considered together because of their intimate association with arthritic changes of the head.

It is unfortunate that the percentage of arthritic changes and aseptic necrosis happens to be the same (33.6 per cent) as the impression is given that all patients with aseptic necrosis had arthritic changes, but this is not the case. Some patients had aseptic necrosis without arthritic changes, and some had arthritis without aseptic necrosis. However, the majority of those with aseptic necrosis had arthritic changes and probably all will eventually have them if weight bearing is carried out over a sufficiently long time.

The arthritic changes in the head were arbitrarily classified as moderate and severe. Under moderate are included those cases with roughening, slight depression, and irregularity of the head, and the severe cases include those in which there has been varying degrees of collapse of the head. Nineteen per cent of the hips (23 hips) showed moderate arthritic changes in the head and 14.6 per cent (18 hips) showed severe arthritic changes. In those cases followed from one to two years only, there was a predomination of the moderate type of arthritis, but as the follow-up extended from two years on to several years, there was an increase of the severe type of arthritis.

Clinically, the patients with moderate arthritic changes have been able to tolerate the pain in the hip for a restricted amount of weight bearing, while those with severe arthritic changes have been definitely handicapped because of pain on weight bearing, having to resort to supports. The time of appearance of arthritic changes seems to follow the time of appearance of aseptic necrosis by several months to a year.

#### FINAL RESULTS

The final results in this series of cases indicate that the average central fracture

of the neck of the femur has the following prognosis: Mortality 9.3 per cent; poor end result, including ununited fractures (13.5 per cent); and severe arthritic changes (14.6 per cent) 28.1 per cent; fair end result (moderate arthritic changes) 19 per cent; good end result, 43.6 per cent. These statistics are not brightened when it is considered that approximately one-half of the patients showing moderate arthritic changes, or a fair end result, had been followed for only one to two years. No doubt, if these cases are followed for an additional period, several will develop severe arthritic changes. In the end, it can be stated that 43.6 per cent will walk well and normally, and approximately 25 to 30 per cent additional will walk with varying degrees of pain, and varying amounts of support.

COMPARISON OF THE WHITMAN METHOD AND  
INTERNAL FIXATION

If these statistics present a rather dreary outlook for internal fixation, consider the study made in 1934 by J. S. Speed at the Clinic of 100 cases of central fractures of the neck of the femur, adequately treated by the Whitman abduction method and traced for a period of at least two years. The purpose of his investigation was to determine the percentage of union of the fractures and aseptic necrosis of the femoral head. A comparison of the end results of Speed's series treated by the Whitman method and the present series treated by internal fixation shows:

	Union Per cent	Non-union Per cent
Speed's series		
(Whitman method)	52	48
Present series		
(Internal fixation)	86.5	13.5
Memphis, Tennessee.		

ASEPTIC NECROSIS

Speed's series	35
Present series	33.6

Internal fixation has apparently exerted a rather profound beneficial effect on the percentage of unions obtained in these fractures, but the percentages for aseptic necrosis so closely coincide that it appears the factors influencing aseptic necrosis are independent of the type of treatment used and

have not been affected either for better or worse by operative treatment.

The mortality rate associated with the Whitman type treatment has been quoted as varying from 20 to 50 per cent and in some cases slightly higher depending on the individual nursing care the patients receive. Internal fixation seems to be a definite improvement from this standpoint. The manipulative and plaster immobilization method offers the further disadvantages of stiffness of the knee joint which often develops, and muscle retraction produces shearing movements with consequent shortening and frequent rotation of fragments. Internal fixation allows the position of the patients to be changed as often as necessary, and they can be allowed to sit up in bed on the day of operation, and if need be, gotten up into a wheel chair in 24 to 48 hours.

Formerly it was generally felt that internal fixation should be reserved for good surgical risks, but with the mortality rate at its present level, and since the greater percentage of fractures (78.3 per cent) occurs past the time of life when they would be considered good operative risks, it is obvious that only a few would benefit by the procedure if this criterion was maintained. Unless moribund on admission, the patient is entitled to the advantages of the operation.

OPTIMAL TIME FOR OPERATION

There is some diversity of opinion as to how long operation should be postponed following the accident. At the Clinic, it has been found highly advantageous to the patients to operate on them within the first 48 hours. A large percentage of the patients arrive within this period. Most all of them have required an opiate for relief of pain, and on arrival, have usually had very little or nothing to eat or drink. Some are vomiting and practically all are dehydrated and in an early state of acidosis. During this period, it is usually fairly simple to restore them to somewhere near the state of health they enjoyed previous to the accident by the use of saline and 5 per cent glucose solution. This is probably the main argument for early nailing at the Clinic. It has also



been found that these elderly patients are not comfortable in traction or splints. Every movement of the hip is painful, and in self defense, they lie quietly on their backs, which invites hypostatic pneumonia and decubitus ulcers. The pain experienced in attempting to move, as in getting on and off the bed pan, has caused the Clinic to adopt the policy of not giving preoperative enemas. Most of them have eaten very little prior to operation, and the enema can be postponed to the second or third postoperative day, at which time it can be given without too much discomfort.

#### TYPE OF OPERATION EMPLOYED

The simple technic of so-called "blind nailing" without opening the hip joint is used in internal fixation of these fractures. Roentgenographic control is used and sodium pentothal is employed almost universally as the anesthetic. The fracture is reduced by manipulation and roentgenograms taken in the anterior, posterior and lateral views to verify the reduction. After routine surgical preparation, a short longitudinal incision is made down to the bone. A guide wire is inserted through the shaft and neck into the head, and if roentgenograms show the wire to be in proper location, the nail is driven in over the wire. Final x-rays are made to check the position of the nail and the wound closed. Operative time varies from 45 minutes to an hour and a half.

Postoperatively, no immobilization is used. Bed rest is usually employed for two months during which time the patient is gotten up in a wheel chair daily. At the end of two months, the patients are up on crutches and partial weight bearing may be started at three months. Full weight bearing is not allowed until union can be demonstrated by x-rays, which varies from less to more than a year.

#### REMOVAL OF THE NAIL

The nail should not be removed until roentgenograms show that solid bony union has occurred with trabeculations across the fracture line. Since this usually occurs at about one year, it is the impression at the Clinic that the nail should not be removed under this time. In nine of the cases of

non-union, the fracture repair appeared to be progressing satisfactorily and the nail was removed at four to ten months post-operatively following which whatever union was present disintegrated, and the fragments separated. These cases occurred in the early 1930's at which time the nail was removed as early as possible. At present, if the nail is causing no difficulty, it may be left in place indefinitely.

#### CONCLUSIONS

1. A sufficient number of fresh central fractures of the neck of the femur has been studied to enable the surgeon to give the patient and relatives an approximate idea or outline of what the future holds for them.

2. Evidence has been introduced to show the superiority of internal fixation over the Whitman method of manipulative reduction and plaster immobilization.

3. It is evident from the data presented that non-unions have been markedly reduced by internal fixation, but the problems of aseptic necrosis of the femoral head, and the treatment of patients with severe degenerative arthritic changes, are still very formidable ones.

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#### DISCUSSION

*Dr. H. T. Simon* (New Orleans): I first desire to congratulate Dr. George on his excellent presentation. I do not know that much could be added along the lines of his presentation. It would be amiss, in discussing internal fixation of hip fractures, not to recall to this audience the fact that many years prior to the Smith-Peterson nail, internal fixation on hip fractures by means of iron (wood) screws was described and used in the City of New Orleans, by Drs. E. H. Parham, and Denegre Martin. This work was elaborated by Drs. Isidore Cohn, Rogers Brewster, Will Bradburn, and many others. Unfortunately, radiographs were not obtainable in operating rooms and shock proof x-ray units were not available when their method

was first described. If such had been the case, I am certain that the internal fixation, as described and practiced by Drs. Parham, Martin, and their associates, would have been more generally accepted by the bone and joint surgeons of this and other countries. I do, however, believe that their pioneer work was of definite help in the evolution of internal fixation of hip fractures.

The problem of treatment of hip fractures has been solved from the standpoint of union but as pointed out by Dr. George, there is still bone necrosis and arthritis with which to contend. It must be remembered that fractures of any joints of older individuals are associated with arthritic changes and dysfunctions, together with discomfort. It is not amiss then to expect these changes in hip fractures. It would also appear impossible to eliminate bone necrosis and arthritis in a certain percent of these fractures.

*Dr. J. T. O'Ferrall* (New Orleans): I am sorry I did not hear the beginning of this paper. It was very interesting and Dr. George's results appear to be about the average with the Smith-Peterson nail. Personally, I am against the nail; I think it displaces too much bone, is more difficult to insert and requires, as a rule, a general anesthetic. Dr. George mentioned that he had used this procedure on one lady 96 years old. I do not believe a general anesthetic is a good thing for these old people. I do not agree with the time at which reduction is essential. I think these people as a rule have a certain amount of surgical shock and reduction should not be attempted for a week or ten days after. I have had several people who needed reduction and nailing who have died while we were waiting for them to recover from the surgical shock; not from pneumonia or heart failure, but purely surgical shock. Among the Mayo men, Dr. Myerding and Dr. Henderson said we should wait two or three weeks, if necessary, to give these people opportunity to recover from shock. So many of the surgeons I know become quite excited and want something done immediately. I think traction is the immediate necessity. I believe the Smith-Peterson nail is too large and displaces too much bone. I think it is shown very admirably in Dr. George's slides how difficult accurate insertion is. I do not believe the bone changes shown in the slides are an arthritis; they are an osteochondritis. It is almost like a case of Perth's disease. In fractures of the hip it is not the head that necroses but the femoral neck that necroses. I do not want to be put in the position of criticizing the doctor just to be criticizing. I think some of his results are excellent but I believe if you can do these cases under a local anesthetic and with multiple pins it is a better procedure. I prefer Bohlman pins with slight modification. You can insert them with a drill. With a Smith-Peterson nail you can hear them being driven in all over the operative floor, and the large nails frequently slip out. I believe mechanically,

it is bad because of the size. I believe if you will put in smaller nails you can do it more quickly and more accurately, and not have a chance of aseptic necrosis, certainly not of the head. The Bohlman pin is not a small pin like the Moore pin. The Bohlman pin has a small hole in the distal end in which you put a wire, and this makes the three pins virtually one pin. If you put them in in three different directions and wire the ends together, I have never had any work out. I have had Moore pins back out, however. I ceased to use those many years ago.

*Dr. M. M. Bannerman* (Baton Rouge): I would like to say that I enjoyed Dr. George's paper and feel that his results as far as mortality reported an accurate picture of the condition. There is one thing I think we should consider very strongly in people with fractures of the neck of the femur: practically any patient with fracture of the neck is entitled to surgery for that condition for these reasons: it will prevent those patients from becoming bedridden, not being able to walk again and from living a life of invalidism from then on out. I think any patient with fracture of the neck of femur, regardless of age and the fact that he might be in shock, barring those cases, at least should have the opportunity for surgery.

*Dr. George* (in closing): I would like to thank Drs. Simon, O'Ferrall and Bannerman. In answering Dr. O'Ferrall, I will say that we have used Knowles pins in the nailing of these hips. They are small pins. We have used three or four pins in a fracture but have never been able to get them in so that the head will stay with the distal fragment of the neck. We have been able to put Smith-Peterson nails in and if there is absorption of the neck, which there is in 11 per cent, the nail backs out. We feel that we get better results with the Smith-Peterson.

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## DOUBLE NOTCHED GRAFT FOR LUMBOSACRAL SPINE FUSION\*

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The treatment of painful lesions of the lumbosacral area of the spine by spine fusion has been attended in the past by failure of fusion in from 15 to 50 per cent of cases. One reason for this failure has been the difficulty in securing proper mechanical fixation of the graft and proper postoperative immobilization of the area

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\*Read before the meeting of the Orleans Parish Medical Society, June 9, 1947 in New Orleans.

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grafted. The spine lends itself poorly to the use of screws and plates, although these appliances have been employed by some authors. Certainly no one believes that the spine can be immobilized rigidly in a cast or any other form of external appliance.

In 1942 Bosworth<sup>1</sup> described a double notched tibial graft for use in lumbosacral spine fusions. Similar grafts have been described by Moore<sup>2</sup> and Breck and Basom.<sup>3</sup> The double notched graft seems to provide rigid fixation of both the graft and the area to be fused in a manner not possible with the usual technics of Hibbs, Albee, and their modifiers.

The technic of the double notched graft is not dissimilar to the usual spine fusion other than the preparation of the graft bed, the shape of the graft, and the use of both iliac and tibial bones. The routine linear incision extending from the second lumbar to the second sacral spinous processes is used. The spinous processes and laminae are exposed by subperiosteal dissection laterally as far as the articular facets. All cortical bone is removed from laminae plates and spinous processes to provide a vascular osteogenetic bed for the grafts. The spinous process of the most superior vertebra to be fused is notched caudally and the lowest spinous process to be fused is notched cephalad. Intervening spinous processes are resected at their bases. The kidney bar on the operating table is raised at this point to place the spine in maximum flexion. The distance between the notches is then measured with a caliper to determine the length of the tibial graft and the depth of the notches in it. A tibial graft of these measurements is cut, notched at each end, with its length between notches exactly the same as the distance between the notched spinous processes. The graft, which is roughly in the shape of the letter "H", is then placed with its notched ends engaging the notched spinous processes. When the kidney bar of the table is lowered, the spine attempts to go into extension, but in so doing rigidly locks the graft in place. In this manner both the graft and the lumbosacral spine becomes rigidly fixed, so rigidly in fact

that one can almost lift the patient off the table by the graft. Iliac bone removed through a separate incision is then placed beneath the tibial graft to provide rapid formation of new bone and consolidation.

Postoperative care is simple. The patient lies on a board bed for two weeks after which he is fitted with a wide lumbosacral brace and permitted to be up and about. The brace is worn for approximately six months, at which time fusion usually is radiographically solid. Bending, stooping and lifting are restricted during this period.

During the past two and a half years this grafting technic has been performed by members of the orthopedic department of the Ochsner Clinic on 34 patients, 24 of whom have been examined six months or more after operation. The entire group of 34 patients represents less than 5 per cent of individuals seen in the department because of pain in the back. In all other patients conservative treatment has been adequate to control symptoms. The primary indication for the operation is pain in the back caused by lack of bony stability or a localized bony lesion and not relieved by conservative measures (table 1). There

TABLE 1  
INDICATIONS FOR SPINE FUSION

Spondylolisthesis	13
Root syndrome (ruptured disk, etc.)	8
Congenital deformity	2
Traumatic arthritis	1
Total	24

were two failures of fusion in the 24 cases, an incidence of 8.3 per cent (table 2). This figure compares favorably with the previously reported percentage of failure of from 15 to 50 per cent.

TABLE 2  
RESULTS OF SPINE FUSION

Functional Result	Cases	Per Cent
Excellent	15	62.5
Good	4	16.7
Fair	2	8.3
Poor	3	12.5
Total	24	
Failures		
Anatomic (failure of fusion)	2	8.3
Functional (psychoneurosis)	3	12.5
Total	5	

Three cases were considered functional failures. The emotional stability of these patients was not adequately evaluated

prior to fusion. All of us realize that low back pain represents one of the most common symptoms of psychoneurosis. Like the remainder of the series these three persons had well defined organic lesions, but their long standing pattern of functional or emotional instability was not appreciated until after operation. All three had successful anatomic fusion which should have relieved their symptoms if they were strictly on an anatomic basis. From their previous histories and subsequent evaluation by psychiatrists, it was shown that on a psychiatric basis alone, these patients should not have had spine fusion. It was after analysis of these functional failures by both the orthopedists and the neuropsychiatrists that it was decided that a preoperative neuropsychiatric examination would be done routinely before performing spine fusions. No operation on patients considered emotionally stable by the neuropsychiatric department has resulted in functional failure.

#### CONCLUSIONS

1. The double notched prop graft for lumbosacral spine fusion will give a higher percentage of successful fusion than other technics.

2. The patient is more comfortable postoperatively since this grafting technic is mechanically stable and does not need plaster casts in the postoperative period.

3. Neuropsychiatric examination of patients before operation is to be recommended as it will give the surgeon some insight as to the expected functional results in elective operations.

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## CONGENITAL OCULAR ANOMALIES RESULTING FROM (a) PREMATURE BIRTH (b) RUBELLA INFECTION OF MOTHER DURING PREGNANCY\* ·

W. R. BUFFINGTON, M. D.

NEW ORLEANS

Congenital anomalies and lesions in premature infants have been seen and recognized as such for many years. But in recent years, saving the lives and lowering the mortality of premature infants is a result of advancement in medicine. Because of this the congenital defects in this group of infants is becoming far more frequent.

Terry, in 1942, refers to a peculiar ocular condition in twins born two months prematurely which he termed premature and fibroplastic overgrowth of a persistent vascular sheath behind each lens. In his cases the membrane did not cover the entire posterior surface of each lens. In other words, after dilating the pupils a clear fundus could be seen.

In infants born sufficiently prematurely, the pupillary membrane can be observed with ease and the presence of the posterior part of the tunica vasculosa lentis and the hyaloid artery can nearly always be seen because they do not disappear until later in fetal life, usually four to six weeks before full development.

Terry states after careful study that the so-called persistent tunica vasculosa lentis consists of a growth of embryonic connective tissue of the tunica vasculosa network in the form of a retrolental fibroplasia. It usually consists of a fibroplastic sheath behind the lens. It is sometimes seen in children born at full term and is usually seen a few days after birth. In full term infants the condition is unilateral. Because of its peculiar appearance, the clinical diagnosis is usually glioma, and the mistake is not discovered until the specimen is examined pathologically.

\*Read before the Sixty-seventh Annual Meeting of the Louisiana State Medical Society, New Orleans, May 14, 1947.



In the report of some of the cases it was found that, at the birth of extremely premature children, the tunica vasculosa lentis was still functioning. This can be observed sometimes four to six months after birth. The following are the changes often seen in this peculiar type of anomaly in the eye of premature infants.

1. As you look through the pupil you see a grayish mass which is the result of the changes due to fibroplasia of the tunica vasculosa lentis.

2. There may be a typical hyperplastic tunica vasculosis. Immediately behind the crystalline lens are seen the hyperplastic changes and behind it is a dark line, the remains of the hyaloid artery, which of course is always connected with the tunica vasculosa lentis in embryonic life. As previously mentioned, in the normal embryo at the end of nine months, the vascularized tissue known as the tunica vasculosa lentis, and the hyaloid artery have disappeared and it is only with a high-powered microscope that the remains can occasionally be seen. But in the premature eye they have not developed the necessary changes to clear up and destroy this embryonic vascularized tissue, hence the reason for the formation of this fibroplastic growth of the tunica vasculosa lentis in premature infants.

Now the question remains as to treatment. It is fortunate, indeed, that we do not have to remove the eyes of these children because there is a certain amount of vision, even if it is not much better than light perception. In looking at these patients it would seem an easy matter to remove the crystalline lens which is generally subluxated backwards by traction, or to make a discission of the fibroplastic tunica vasculosa lentis behind the lens. Some operators have obtained good results but in most cases the operative results have not been very favorable. Radiation has been tried but has proved valueless. In removing the lens or doing a discission, very often a persistent glaucoma will result.

Reese and Payne reported similar cases, with the complications which later de-

veloped. Some had early intraocular hemorrhages, other later in life developed glaucoma for which operations had to be done. They also called attention to the fact that these congenital anomalies can be clinically taken for glioma. Of these cases, 12 had to be operated on for glaucoma. In two or three patients, however, the membrane was opened up, the opaque lens removed, and there seemed to be an improvement of vision in the operated eye. It is remarkable and fortunate that these premature babies develop a normal mentality. The twins I am reporting show all the evidence of being normal in every way except the ocular defect.

#### CASE NO. 1

In 1945, was born prematurely at seven or eight months, a four and a half pound boy. He was kept in an incubator for a time. It was discovered a little later that something was wrong with both eyes. A very competent oculist in another city made a diagnosis of advanced bilateral glioma, advised removal of the eyes. I saw the child in consultation. After dilating the pupils, the baby was given an anesthetic. On examination it could be seen that the condition in both eyes was a peculiar thick disc-like membrane behind each lens. Seemingly, the lenses were slightly subluxated, so we came to the conclusion that it was a typical case of bilateral retrolental fibroplasia. I had occasion to see this boy for some time and condition remained absolutely stationary. Slight subluxation of the lenses I think results from the traction of the retrolental fibroplasia.

#### CASES NOS. 2 AND 3

Twins, V. M. and D. M., born prematurely at seven months, weighed three and a half and four pounds respectively. They were in an incubator five weeks. Four months after birth, parents noticed evidence of defective vision and they consulted Dr. Lorio. I quote a letter from Dr. Lorio on these cases:

"I am referring to you D. and V. M., age six months, twins. These were premature children (seven months). Everyone in the family healthy. I first saw them today, three of the eyes looked exactly alike but the left eye on one seemed less involved so I put a drop of atropine in the left eye and a drop in the right eye of the other child. Examination showed a white substance filling the posterior surface of the posterior chamber. On the left eye examined the retina could be seen on the nasal side but bulging into the posterior chamber, from the temporal side, could be seen a very definite mass. After finding this condition I

realized that I would go no further without consultation; therefore, I would not examine under anesthetic as you might want to do the same and this would have subjected them to two anesthetics. I do not know of any disease except glioma that looks like this, but treatment being so drastic if it is glioma, I would not advise without a consultation. I have never heard or read of four gliomas in twins, yet that would be my diagnosis."

These children were first seen by me October 10, 1946. The grayish mass as noted by Dr. Lorio was very evident. They had all the appearance, therefore, of being either a tumor extending up from the posterior aspect of the eye, or being a dense, peculiar, opaque, irregular membrane behind the lens. They were again seen in January, 1947. V., at that time, showed that right eye anterior chamber was shallow, lens opaque and disc-like in shape and dislocated upward and slightly inward. The iris was not tremulous. Left lens was dislocated temporally and the fundus could be seen distinctly through the dilated pupil. There seemed to be some peculiar congenital anomaly in and about the optic disc but he does have evident light perception.

D., at that time, also showed shallow anterior chamber, pupils dilated 4 mm., right eye, lens subluxated up and nasally, left lens dislocated directly backwards. The lenses were becoming opaque but the sheath of fibroplastic tissue was seen distinctly behind it. These eyes likewise seemed to have a certain amount of light perception. The lenses are dislocated backward I think due to the traction made by the retrolental fibroplasia. When seen in January and again the last time in April, 1947, it had become evident that the abnormalities in the eyes of the two children were not glioma and it would not be necessary to remove the eyes, hoping that there might be saved a certain amount of vision.

#### CONGENITAL ANOMALIES FROM RUBELLA INFECTION OF THE MOTHER DURING PREGNANCY

In 1941, following an epidemic of rubella or German measles in Australia, Gregg, of that country, reported a large number of children with congenital cataract born of mothers who had rubella in the early weeks of pregnancy. Gregg's report is based on 20 cases of his own and 58 reported to him by colleagues. In these cases most babies were small and ill-nourished and difficult to feed.

All babies had cataract from birth, all were bilateral except 16. In most cases the opaque lens was pearl grey. Nystagmus became manifest after three months.

Five per cent of the 78 cases had congen-

ital heart lesions. In the series early death was recorded in 15. It was noted without exception that there was a marked intolerance to atropine.

#### ETIOLOGY

Based on the date of birth of each one of the series affected and the history given by the mothers, it was noted that the larger percentage came from mothers who had suffered from German measles in early pregnancy, usually in the first or second month. In some instances the mother did not realize she was pregnant at the time of the infection.

In 1944, Reese reported three cases. All three had congenital cataract and congenital heart lesions. All mothers contracted rubella during the first month of pregnancy. He advises early operation since it is noted that nystagmus does not come on until after three months in most cases.

Long and Danielson call attention to 61 women who contracted German measles during pregnancy. Forty-one bore children with congenital defects. Of these 15 had cataracts. They report six cases with cataract. All the mothers had the measles during the first six weeks of pregnancy. All six cases had, in addition to the cataract, some type of cardiac lesion. These cases showed some evidence of micro-ophthalmus.

Cordes and Barker state that since publication of Gregg's paper 170 cases of rubella during pregnancy have been reported, 125 of which, or 75 per cent, were followed by congenital cataract or lens defect in the child. In all these cases the mother contracted rubella during the first three months of pregnancy. One case had a lens defect reported after the third month.

Goar and Potts report five cases seen and operated. They also advise early removal of the cataracts.

Krouse reviews the reports of Swan in a series of 74 cases covering the years 1939 to 1943. In these cases a definite history of rubella in 61 mothers during pregnancy showed 20 infants had no ocular or other lesion. The mothers of these infants had rubella late in pregnancy. Of 41 infants who had congenital ocular and other defects,



the mothers dated the rubella before the fourth month. The leading congenital anomaly was the eyes, notably cataract, when the mother became infected three weeks to three months after pregnancy.

Finally, Rones reports that The State of Australia, after Gregg's report, sent out a committee to investigate the matter. The committee's conclusion was if a woman contracts rubella in the first two months of pregnancy, chances for giving birth to a congenitally defective baby were almost 100 per cent.

Statistical data accumulated since Gregg wrote his paper have proved that children of mothers who have contracted rubella or German measles after the fifth month are usually free from these peculiar anomalies. There has been no treatment which could be given the mother in the form of vaccine or otherwise, which could prevent these defects in children. It would be interesting for us to study the effects of other contagious diseases on the embryo.

I wish to report the following cases which belong to this group:

#### CASE NO. 4

This patient was first seen December 17, 1943, aged 10 months, with a right and left cataract since birth. The mother gave a history of having German measles eight months before the baby was born. Immediately after birth, the child had to be given nine transfusions. She was also given vitamin K for petechial hemorrhages. She had no congenital cardiac lesion. Slight microcornea, nystagmus, pupils active, pearl grey opaque lenses in both eyes. On May 9, 1944, a discission was done on the right eye. On June 13, 1944, a second discission was done on the same eye. On August 15, 1944, a discission was done on the left eye. In both eyes the lens were found to be undeveloped. Because of lack of cooperation, it was impossible accurately to determine the visual acuity. Approximately + 13.00 sph. is about the correction of each aphakic eye. Her vision is definitely imperfect, due to congenital amblyopia.

#### CASE NO. 5

Baby H., 6 months, seen in consultation. A diagnosis was made of: (1) congenital bilateral cataract, (2) pediatrician found baby had definite congenital heart lesion. It will be wise to remove the cataract within the first six months. In the light of our present knowledge we must be cautious in giving a prognosis. Other congenital ocular defects may be present as in Case 4.

When to operate on these babies is important. Some doctors suggest early operations, others believe that because of the low resistance of these infants, operations should be delayed. In my opinion, the cataract should be removed just as soon as the child has normal resistance. This usually will take place within three to six months after birth.

#### DISCUSSION

Dr. Paul L. Marks (Baton Rouge): This little baby Dr. Buffington saw was a full term child. The mother had rubella when between seven and eight weeks pregnant. She had two other children who contracted it and gave it to her. When the child was born he weighed slightly more than five pounds. In addition to having what is thought to be a congenital heart lesion the little boy has a thyroglossal duct cyst. I had hoped to operate when he was about four or four and a half months old, which would be within the next week or so, but unfortunately the child got chickenpox this week so we will have to postpone this somewhat. I have made an effort to dilate this child's pupils with 2 per cent homatropine and paradrine. One pupil dilates very well; the other does not. In the one that does not I have used several other things with an equal amount of no success. I therefore plan to operate on the eye with the better dilated pupil first. The two cataracts are not the same. One is far more complete than the other. The one more complete is the one in which the pupil does not dilate well. When the child was three months old he developed nystagmus in each eye and had definite convergent squint at that time. I think he would be better off if he could have been operated sooner. It is not a good prognosis but we hope for the best.

Dr. N. T. Simmons (Alexandria): Dr. Buffington has brought something to our attention in his usual comprehensive and illustrious manner and leaves very little to say. It is a new subject comparatively speaking and very few statistics have been compiled on it. Some definite statistical studies should be made and after observation and consultation with the pediatricians, cardiologists and possibly the neuropsychiatrists, an attempt should be made to determine if German measles is a justifiable cause of interruption of early pregnancy. While this seems radical today it may be found advisable after a thorough statistical study by the various branches of medicine concerned.

I can not add very much to the subject other than to agree with what Dr. Buffington has said. We all see gliomas and pseudogliomas and frequently are undecided whether to diagnose it glioma and enucleate or to wait and observe it longer. No one wants to enucleate an eye but at the same time if it is glioma and you do not enucleate you

will regret it later. I have taken advantage of Dr. Buffington in the past by having him see these patients in consultation, letting him decide what is best to do.

Dr. Charles A. Bahn (New Orleans): We are indebted to Dr. Buffington for presenting several interesting diagnostic and pathologic problems. Retrolental fibroplasia is a degenerative process resulting from interference with normal structural and functional fetal development. Its differential diagnosis is based essentially on its being non-inflammatory and stationary, and on the frequent association with other ocular and extra-ocular evidences of interference with normal development. Retinoblastoma and endophthalmitis are progressive or inflammatory. Cataracts associated with a rubella maternal infection during the first three months of pregnancy are diagnosed by the history of infection, the distinctive types of lens opacities, and by extra-ocular sequelae especially cardiac lesions, microcephalus and deafness. The unborn child is protected from most maternal infections. In measles, chickenpox, and possibly other virus diseases, this protective mechanism does not usually exist during the first part of pregnancy, and in syphilis does not exist throughout pregnancy. It is therefore important that all expectant mothers be advised to avoid all possible contact with measles and immunized if exposed. The advisability of therapeutic abortion is a responsibility which must be seriously considered.

Dr. M. C. Wilensky (New Orleans): I would like to ask a question: Has anybody ever done any statistical work as to how many mothers with measles have normal babies? I think we should ask obstetricians and pediatricians to report mothers with measles during pregnancy and who give birth to normal children.

Before we can feel sure that measles is the causative factor, we need to compare more statistical evidence as to the incidence of cataracts and other congenital defects in infants born of mothers who had and who did not have measles during early pregnancy.

After all we know a number of infants with congenital cataracts or other defects are born of mothers who did not have measles during pregnancy.

Dr. Buffington (in closing): This has been brought out clearly, that if the mother is pregnant and contracts measles during the first four to eight weeks, the congenital anomalies like cataracts and other changes in the new born occur in nearly a hundred per cent of them. That is so striking that there is something showing definite relationship between the infectious diseases and ocular manifestations. Further, Gobbels took statistical data on 50 or 60 cases with German measles after the fifth month and in those cases the children were all born normally.

## INTRAVENOUS ETHER\* (DIETHYLOXIDE)

USE IN THE TREATMENT OF CASES OF  
IMPENDING GANGRENE AND IMPAIRED  
CIRCULATION

O. C. WILLIAMS, M. D.†

NEW ORLEANS

In February of 1946 I attended a meeting of the Orleans Parish Medical Society and heard Dr. Robert Katz read a paper, giving his experience with the use of ether (diethyloxiide) as a treatment for cases of impending ischemic gangrene. This preliminary report was discussed by Dr. Rudolph Matas. The report was published in the *New Orleans Surgical Journal* of June 1946, giving the results of the use of ether, by the intramuscular and intravenous routes. It is noted in the reprint that Dr. Katz has mentioned the work carried on at the U. S. Marine Hospital at New Orleans by Dr. A. H. Lawton and myself in the intravenous use of ether for treatment of impending ischemic gangrene cases.

After hearing Dr. Katz's preliminary report, I became interested and with the consent of our Commanding Officer I contacted Dr. Katz and with his help started treating our first case March 1, 1946.

I have been asked to present to you this evening the results we have obtained. To date we have completed treatment on 21 patients, and have one in the hospital at the present time receiving treatment. This patient is now on his 24th bottle, and this makes a total of 22 cases in our series.

I realize that the number is small, but I believe our results from the use of the drug are well worth reporting. We have used a 2½ per cent solution of ether, namely, 25 c. c. of stock ether to a 1000 c. c. of 5 per cent glucose in distilled water or in normal saline, in all of our cases. The 1025 c. c. of solution is given daily, intravenously, starting the flow at 40 drops per minute, and if no reaction stepping it up

\*Read before the Orleans Parish Medical Society, February 10, 1947.

†From U. S. Marine Hospital, New Orleans, Louisiana.



to about 50 drops per minute, but not over 60 per minute. We decided that 12 bottles would represent a course, and then give a few days rest, and repeat all laboratory tests before starting on a second course.

All patients were thoroughly studied prior to treatment. This consisted of a careful history, complete physical examination, including a chest x-ray and an x-ray of extremities for evidence of sclerosis, a P.S.P., B.S.P., N.P.N., blood chloride cholesterol icterus index, blood sugar, cephalin flocculation, a.g. ratio Wallace Diamond, sedimentation rate and complete blood count determination. Kodachrome plates were made of the extremities. All of the laboratory tests were repeated after a course and the picture was also repeated.

Blood pressure readings and pulse and temperature records were made during the administration of the drug.

The first patient upon whom we used the drug, was a 62 year old seaman who was admitted to the hospital in December 1944, with the diagnosis of general arteriosclerosis, and gangrene of the toes of the left foot. Sympathectomy was done on December 18, 1944. The result was poor, making it necessary to amputate the left leg, at mid-thigh, January 5, 1945. The latter part of February 1946 the patient developed redness of right foot with beginning gangrene. We started I.V. ether on this patient March 1, 1946. He had a total of 37 bottles; however, we were unable to save the right foot and amputation, Callander, was done April 6, 1946. His postoperative recovery was uneventful, and the amputation stump is well healed. Although the intravenous ether did not save this patient's foot, we noticed that it gave him relief of pain.

We continued using the treatment on cases of impending ischemic gangrene, but did not limit our treatment to this type of case alone. The following is a compilation of types treated.

#### TYPES OF CASES

Thrombo-angitis obliterans.....	9
Diabetic ischemic limb.....	1
Arteriosclerosis .....	5
Ulcer, hypostatic.....	5
Neurodermatitis .....	1
Neuritis .....	1

All of our patients were males and the average age was 47.3 years, the oldest 64 and the youngest 19. The best results were obtained with patients with Buerger's disease and the diabetics. We have estimated our results as good, fair or poor based on subjective findings and objective proof of improvement. We were unfortunate in not having a thermographic machine, which might have given more concrete evidence of improvement.

#### RESULTS OF TREATMENT

	No.	Good	Fair	Poor
Thrombo-angitis obliterans	9	8	0	1
Diabetic ischemic limb	1	1		
Arteriosclerosis	5	3	1	1
Hypostatic ulcer	5	3	2	
Neurodermatitis	1	1		
Neuritis	1	1		

#### SIDE EFFECT FROM TREATMENT

Emesis .....	2
Euphoria .....	0
Drowsiness .....	0
Excitement .....	0
Hysteria .....	0
Convulsions .....	0
Extravasation of solution into tissue of arms .....	1

There was no change in the blood pressure readings, pulse, and respiration in the first 21 patients treated. The majority of these received nicotinic acid during the treatment. The patient now under treatment has received no nicotinic acid and rise in the blood pressure occurs during each infusion.

In only one case was there a change in any of the blood chemistry determinations. This patient showed a slight increase in B.S.P., but it promptly improved with intravenous glucose and later checks have revealed normal findings.

#### CASE REPORTS

Cases No. 2, 3, 4, 9, 10 of Buerger's Disease had received surgical treatment before the administration of ether. Cases No. 5, 6, 7, 8 had not received surgical treatment.

No. 1. Male, white, age 64. Reported in paper. Arteriosclerosis with gangrene.

No. 2. Male, white, age 35. Admitted January 12, 1946. Diagnosis: Buerger's; ulcer of stomach. Chief Complaint: Cold and painful hands and feet. Duration 3 years. 1½ years ago gangrene of 2nd toe, right foot. One year ago had bilateral sympathectomy and amputation of 2nd toe. No sweat-

ing of leg now. Continues to have pain. Cyanosis of fingers and toes. No dorsalis pedis pulse. March 16, 1946—10 bottles of ether solution and nicotinic acid 200 mgm. t.i.d. Discharged April 5, 1946, free of pain in feet; hands were warm, and color good. All laboratory findings were negative. Seen as an outpatient on September 28, 1946—no pain in legs. Free of symptoms.

No. 3. A. B., Male, white, age 59. Admitted March 9, 1946. Diagnosis: Buerger's—since 1927. Intermittent claudication. 1923 sore on right foot, amputation mid-thigh right. Pain in left leg has increased past 14 years. Refused sympathectomy for left side 1941. Sores developed on ankle. Numbness and pain in 5th finger each hand. Leathery feel to skin left leg. Dorsalis pedis pulse absent. Scaling ulcer present. Toes cold and cyanotic. Negative laboratory findings. March 16, 1946—23 bottles of ether solution with nicotinic acid 200 mgm. t.i.d. Discharged April 10, 1946. Results good. Discoloration of leg cleared. Pain and tingling subsided. Ambulatory without claudication. Foot pink and warm. Relief in two days after treatment started.

No. 4. B. W., Male, white, age 35. Admitted March 13, 1946. Diagnosis: Buerger's. Chief complaint: Cramps in leg. In August developed a pain in left foot. Examined in Galveston and New Orleans with an instrument and told he had Buerger's. Had lumbar sympathectomy block with lasting relief one month. Pulse present. Continues to have cramps in leg. Laboratory findings and x-ray negative. March 25, 1946—22 bottles of ether solution with nicotinic acid 200 mgm. t.i.d. Discharged April 20, 1946. Good results. Free of pain. No claudication after long walks. Seen as an out-patient on November 25, 1946, free of symptoms. Has returned to duty.

No. 5. D. L., Male, age 51. Admitted June 28, 1946. Diagnosis: Buerger's and ulcer. Frost bite 1918. 1926 intermittent claudication continued 1940. Has had ulcer intermittent on 2nd toe, right foot, past 12 years. Received treatment of various types without success. Laboratory findings negative. Ulcer was present on 2nd toe and was painful Ether solution, 24 bottles, started July 6, 1946. There was complete healing of the ulcer, and freedom from pain when discharged July 31, 1946. Seen January 1947 and is well. No nicotinic acid.

No. 6. G. G., Male, white, age 61. Admitted May 2, 1946. Diagnosis: Buerger's and ulcer. Unhealed ulcer right ankle. Pain in legs on standing and walking, poor pulse. Laboratory findings and x-ray negative. EKG negative. A course of ether solution of 8 bottles was started May 13, 1946, and nicotinic acid was given. Discharged June 1, 1946, ulcers healed, no pain on long standing or walking.

No. 7. B. R., Male, white, age 31. Admitted July 28, 1946. Diagnosis: Buerger's. Angiospasm with

gangrene of 2nd toe, left. Blister on toe six weeks prior to admission, became worse. Reduced pulse in dorsalis pedis. August 5, 1946 treatment was begun—24 bottles ether solution and nicotinic acid. Never free of pain but became dry gangrene. Sympathetic block September 18, 1946, results good; sympathectomy, left September 23, 1946, results good. Final amputation 2nd toe, left, October 9, 1946. Discharged, well healed, free of pain November 21, 1946.

No. 8. W. C., Male, white, age 61. Admitted February 7, 1946. Diagnosis: Buerger's with burns; Arteriosclerosis, general. Burns of feet and ankles—4 days duration, 1st, 2nd and 3rd degree. Burns healed, pain continued. Heavy smoker. Told he did not have pulse in foot 1 year ago. Skin brawny. Intermittent claudication. Treatment consisted of 24 bottles ether solution with nicotinic acid March 29, 1946. Second course—12 bottles April 29, 1946. Discharged May 16, 1946, results good, burns healed, no pain after long walking. Slight increase in B. S. P., which cleared with I.V. glucose. Readmitted August 13, 1946. Free of pain.

No. 9. J. McK., Male, white, age 56. Admitted February 5, 1946. Diagnosis: Buerger's and gangrene. Chief complaint. (Buerger's disease)—Pain in legs since World War I. In 1941—Amputation of little toe, right foot. In 1941 right leg amputated, mid-thigh. Some numbness of toes at times and also bouts of pain. Developed sore on tip of 4th toe, left foot. Left foot cold. Dorsalis pedis and posterior tibial pulses not felt. Sore on 4th toe. Ether solution begun on March 1, 1946, using 46 bottles—Nicotinic acid 200 mgm. t.i.d. Discharged June 17, 1946, no pain, no gangrene. Hand and foot warm. Pulses present in foot. Only slightest of tingling in toes on prolonged walking. Nails growing.

No. 10. T. T., Male, white, age 26. Admitted June 25, 1946. Diagnosis: Buerger's, and varicose veins. Chief complaint: Pain in legs. Intermittent claudication since 1941. Lumbar sympathectomy, bilateral, 1943. Relief of symptoms. Recurred in 4-5 months. No pulses felt in left foot. Ether solution begun on July 6, 1946, using 16 bottles—Nicotinic acid. Discharged July 24, 1946, good results. Feet and legs warm. No claudication. Patient cheerful.

No. 11. A. G., Male, white, age 19. Admitted March 19, 1946. Chief complaint: Ulcers of ankles won't heal. He had ligation of veins and other therapy without results. Diagnosis: Large ulcers both legs, region of ankles. Ether solution begun April 22, 1946, using 12 bottles. Ulcers practically healed. May 14, 1946, transferred to medical service because of pre and post. treatment. Electrocardiograms showed cardiac damage—right bundle branch block. Had nicotinic acid.

No. 12. E. R., Male, white, age 50. Admitted



September 19, 1945, with recurrent indolent ulcers. Has had various treatment including sympathetic block. Ether solution begun April 20, 1946, using 24 bottles and nicotinic acid with various forms of local therapy. Ulcers healed, patient deserted June 29, 1946.

No. 13. J. G., Male, white, age 36. Admitted July 8, 1946. Indolent ulcer failing to heal. Treatment begun on July 14, 1946, using 14 bottles with nicotinic acid. Discharged July 31, 1946, ulcer completely healed. Extremities warm.

No. 14. G. G., Male, white, age 40. Admitted October 18, 1945, with recurrent indolent ulcer of left leg. Ether solution begun on April 20, 1946, using 24 bottles with nicotinic acid. Discharged August 12, 1946, ulcers completely healed. No pain in legs.

No. 15. J. L., Male, white, age 45. Admitted September 24, 1946. Recurrent indolent ulcers of legs. Ulcers since 1937. Various therapy. Ether solution begun October, 1946, using 21 bottles, ulcers healing. Had extravasation solution into tissue of arms. Patient left the hospital December 18, 1946. Seen in out-patient department regularly since discharge and there has been definite improvement.

No. 16. E. S., Male, white, age 48. Admitted February 1, 1946. Diagnosis: Neurodermatitis. Chief complaint: Burning and itching of left leg—6 months duration. Local therapy and several caudal anesthetics did not relieve or heal. Ether solution begun on April 26, 1946, using 24 bottles and nicotinic acid. Lesions decreased in size. Pain, itching and burning subsided. Finally discharged July 14, 1946, completely relieved of symptoms and fit for duty.

No. 17. J. F., Male, white, age 67. Admitted May 14, 1938, with alcoholic neuritis. Has been here since 1938 and developed pains in legs which responded to five bottles of intravenous ether solution.

No. 18. L. G., Male, white, age 67. Admitted June 17, 1946. Diabetic gangrene 2nd toe, left foot, severe. Marked redness and swelling of the dorsum of foot. Treated with insulin and diet. Gangrene spread. Started intravenous ether 2½ per cent June 22, 1946. Received total of 33 bottles by July 24, 1946. Second course started August 5, 1946, receiving 16 bottles. Gangrene of 2nd toe turned into dry gangrene with application of ether. Ulceration spread to plantar surface of foot; 2nd toe amputated and ulcer area of plantar surface healed. Discharged Feb. 5, 1947, ambulant. Had nicotinic acid.

No. 19. M. Z., White, male, age 56. Admitted Feb. 8, 1946. Diagnosis: Arteriosclerosis. Possible Buerger's. Pain in legs after walking. Intermittent claudication past seven months. Both feet cold. No pulses present. Ether solution begun on March 25, 1946 using 24 bottles with nicotinic acid. Discharged April 20, 1946—completely relieved of

symptoms. Seen as out-patient in November 1946 and had no complaints.

No. 20. M. L., Colored, male, age 48. Admitted May 3, 1946. Onset present illness April 30, 1946. Gangrene of foot. Examination revealed severe moist gangrene involving all toes and part of right foot. Laboratory tests all negative. X-ray negative for sclerosis. Patient started on intravenous ether May 18, 1946, received 24 bottles. Relieved of pain and the gangrenous condition improved to some extent, but took turn for worse and amputation right leg Callender type done June 17, 1946. Patient well until September 10, 1946, at which time developed gangrene of left foot. Treated by refrigeration. Died October 11, 1946.

No. 21. B. W., White, male, age 54. Admitted to hospital June 14, 1946. Diagnosis: Bilateral bunion and severe hallux valgus, bilateral with marked over-riding great toe. On July 12, 1946, McBride type of operation for correction of above deformity was done. Gangrene developed in great toe, left foot. Laboratory examinations all run and found to be negative. Marked arteriosclerosis present. Started on intravenous ether July 20, 1946. Received 24 bottles without nicotinic acid. The gangrenous toe was turned into a dry gangrene and patient lost distal end of great toe but the gangrenous area of foot healed well. Discharged October 1, 1946, wound well healed.

No. 22. O. G., White, male, age 55. Admitted January 17, 1947. Diagnosis: Gangrene right great toe. Patient dropped a small piece of iron pipe on right foot January 14, 1947. The injury was of minor nature, however, great toe became black and also painful.

Examination on admission revealed advanced gangrene of entire great toe, right foot, with marked inflammation of dorsum of foot. Foot cold to touch. Absence of dorsalis pedis pulse. Intravenous ether started January 17, 1947, and has received 24 bottles to date. The inflammation has all subsided. The gangrenous area is now limited to the distal half of the great toe and is dry type of gangrene.

Patient has been relieved of his pain, the foot is warm out to the gangrenous area.

This patient will be given a few days rest. The laboratory tests will all be repeated. Kodachrome pictures will be repeated and if patient shows no change in laboratory tests a second course will be started.

Nicotinic acid has not been used in this case and it has been noted that there is a rise in the blood pressure during each infusion of the ether mixture. The second course of ether will be supplemented with nicotinic acid.

#### SUMMARY

1. Report is made of the use of intravenous ether in treatment of 22 patients with impending ischemic gangrene, dia-

betic ischemia, arteriosclerosis, hypostatic ulcer, etc.

2. It is recognized that the series is small, but results have been encouraging.

3. Relief from pain has been one of the most gratifying findings.

4. The ether treatment has not been unpleasant to patient.

5. Ether is considered a safe drug to use in the dilution that we administer it.

6. We consider it a valuable agent. It can be given while patient is being prepared for surgery when this becomes necessary.

8. Cases should be carefully observed and evaluated prior to treatment.

#### REFERENCE

Robert A. Katz, M. D., Impending ischemic gangrene. New non-surgical therapeutic suggestions. New Orleans Surgical Journal, pp. 542-555, Vol. 98, No. 12, June 1946.

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## FRACTURED RIBS FROM COUGHING

J. M. BODENHEIMER, M. D.

SHREVEPORT, LA.

Fractures of the ribs without direct external trauma have been reported rarely in literature. However, many writers think that the injury occurs more commonly than the records would lead one to believe. Wahl, who reported four cases, collected 63 cases from the available literature. Bahr collected 35 cases. The first case of spontaneous rib fracture was reported by Graves in 1834. Coughing and sneezing are the usual causes of this injury. Popisichill found 12 cases among 25,000 children suffering from whooping cough. Oechsli, Richardson, Tunis and others have reported fractures associated with pulmonary tuberculosis. Swingord & McKinnon reported one case in which eight fractures of ribs were identified by x-ray. Ribs on both the right and left side were fractured. Most fractures are about the same distance from the spinal column. An occasional anterior fracture is observed. Of the fractures reported about 76 per cent were on the left side, 20 per cent on the right side, and four per cent on both sides. According to Bahr, the liver weakens the trauma effect, hence the greater number found on the left side.

Congenital anomalies may account for some of the accidents. Osteomalacia, rickets, lues, tuberculosis and malignant diseases of the ribs (primary or metastatic), multiple myeloma, Ewings tumor, hyperparathyroidism, senile osteoporosis, Paget's disease and osteomyelitis are mentioned in literature as predisposing causes. Excessive muscular force, coughing, laughing, sneezing, parturition and excessive weight lifting have been reported as the exciting causes in various case reports. However, the most common exciting cause is coughing.

A sudden pain over one or more ribs following any of the above mentioned exciting causes, and which persists with localized points of tenderness over a rib or ribs, leads to a suspicion of fracture. Roentgenographs taken at proper angles will show the fractures if they exist.

The treatment is no different from the usual treatment of fractured ribs.

The following case is reported:

#### CASE HISTORY

Mr. S. L. F., age 67 years, came to the office complaining of severe pain on the left side anterior just under the ribs. The pain was unrelieved by diathermy or opiates. The cough which was persistent and due to an acute upper respiratory infection aggravated the pain. After several days of treatment, a cutaneous hemorrhagic spot the size of the palm of the hand was noted. The hemorrhage continued to spread until it involved the entire surface of the left half of the abdominal wall, and later spread to the outer surface of the thigh and across to the right side of the abdomen before it was arrested. There was no history of previous spontaneous bleeding. He did not smoke or drink. He was considerably overweight, a family tendency aggravated by over-eating.

There was edema of the lower extremities and the abdomen contained some fluid. The urine showed a trace of albumin, hyaline and granular casts. The blood picture was normal except that the platelets were 150,000 per cc. The bleeding and clotting time were normal. NPN was 62, icterus index 86. Several days later the NPN was reported 29. The first x-ray report was negative for fractures of the ribs. Later the x-ray taken at oblique angles showed two fractured ribs posterior and one anterior.

A specimen of the rib at the anterior fracture was removed under local anesthesia and submitted to Dr. W. R. Mathews, pathologist, for examination. He reported the following:



*Specimen:* Tissue from upper abdominal wall in vicinity of costal margin. *Date:* 12-31-45. *Gross:* The specimen consists of the tip of a rib (cartilagenous portion) with fragments of soft tissue showing a grayish yellow color. *Section.*

*Microscopic:* 1-2-46. The sections from the cartilagenous tip of the rib show no deep change so far as inflammatory reaction is concerned. However, in some of the sections there is small centrally located irregular cystic space that appears to have developed by dissolution of the cartilage. The perichondrium shows marked chronic productive inflammatory reaction with a number of areas of newly formed osteoid tissue in this zone. The reaction here is almost entirely productive in type (fibroblastic) though a few lymphocytes are present, usually focally. The blood vessels are not numerous and their walls are well formed. As one proceeds from the rib into the surrounding soft part, the structure is mainly that of low grade inflammation in fat. There has been pooling of fat spaces with intervening foci of foam cells (fat regeneration) in association with a varying amount of fibroblastic reaction and slight round cell infiltration. The margins of some of the pieces containing quite a number of capillaries looks like granulation tissue but only an occasional polymorphonuclear leucocyte is present. On the fringe of the section the fibroblastic and lymphocyte reaction is noted to be extending out into the adjacent striate muscle.

This is an inflammatory process involving the perichondrium and surrounding soft tissue but there are no specific features as to etiology so far as I can tell. The best diagnosis that I can make is perichondritis but I don't know what caused it. It could be a complication of some infectious disease. I fail to find an explanation for the expanding hemorrhage in the anterior abdominal wall. It is assumed that there was no trauma to this area.

The treatment consisted of bed rest, opiates, dry heat, vitamin K, salt free diet, Salyrgan and Theophyllin. The side was strapped with adhesive plaster, but as the skin would not tolerate it, the strapping was discontinued. The fractured ribs event-

ually healed, the edema subsided and the kidneys cleared. The blood picture returned to normal.

Though this condition is rare, it is well to emphasize the fact that persistent pain and tenderness localized over one or several ribs and accompanied by a resistant cough, should be investigated for possible fractures. It might be added that unless the x-ray is properly taken the fracture or fractures can be overlooked. This is well emphasized in the case report. The first x-ray taken was negative for fractures; the subsequent x-ray examination taken at proper angles revealed clearly the fractures.

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## SULFONE TREATMENT OF LEPROSY

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Sulfone drugs were first used in the treatment of leprosy by Faget and co-workers<sup>1</sup> at the National Leprosarium, Carville, Louisiana in 1941. Sulfa or sulfonamide derivatives (sulfanilamide, sulfathiazole, sulfapyridine, and sulfadiazine) had previously been demonstrated as ineffective drugs in leprosy except for varying degrees of usefulness in clearing up secondary infections of skin and mucous membranes.<sup>2</sup>

Promin (sodium salt of p.p. diaminodiphenyl sulfone n.n. didextrose sulfonate) was the first drug of the sulfone series to be used in leprosy. Its reported value in experimental tuberculosis in guinea pigs<sup>3</sup> and its seemingly promising clinical trial at that time in human tuberculosis<sup>4</sup> led the Carville workers to try this drug and continue its use in leprosy. Results at first were not very promising. Following the methods by which the clinical trial of pro-

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\*Read before the Orleans Parish Medical Society, October 13, 1947.

min was being carried out in human tuberculosis, the drug was administered orally. Toxic symptoms following oral administration were severe. Dosages had to be kept so low that therapeutic effects seemed unlikely. Oral treatment with promin was abandoned in favor of a promin-like drug called Internal Antiseptic No. 307 which was well tolerated orally.

Internal Antiseptic No. 307 (sodium 4,4'-diaminodiphenyl sulfone-2-acetyl sulfonamide) was administered to one group of patients while a placebo was given to another group of patients.<sup>1</sup> After 8 months of treatment the group that received I. A. No. 307 was in a much better condition as far as this group of patients' specific leprous lesions and complications were concerned. This indicated that the improvements in leprosy under this promin-like drug could not be attributed to spontaneous regression of lesions but to some added factor, in this case I. A. No. 307. Meanwhile, a preparation of promin suitable for intravenous use had been perfected. Toxic manifestations following intravenous administration were surprisingly mild; so mild that several times the original dosage was perfectly well tolerated by most patients. Improvement in specific leprous lesions and leprous complications was considerably accelerated over that obtained with I. A. No. 307. I. A. No. 307, consequently, fell by the wayside before it really had had an adequate clinical trial.

When it becomes necessary to administer a drug daily intravenously to a large group of patients a number of administrative and technical problems arise. A search, therefore, was made for a drug with a therapeutic action comparable to promin but which could be administered orally with minimal toxic effects. Such drugs were found in diasone (disodium formaldehyde sulfoxylate diamino diphenyl sulfone) and promizole (4,2' — diaminophenyl — 5' — thiazole sulfone). These drugs, like promin, were also being evaluated in the treatment of human tuberculosis.<sup>5, 6</sup> Therapeutic results as well as toxic effects from these two drugs were found to be comparable to that

of promin with the added advantage that they were tolerated well orally while promin was not.

The investigations conducted by the Carville group<sup>7, 8, 9</sup> with the sulfone drugs in leprosy have been confirmed subsequently by a number of leprologists of other countries. Muir's<sup>10</sup> experience with diasone in the British West Indies "so far corresponds closely with those reported on the use of promin at Carville". Fernandez and Carboni of Argentina<sup>11</sup> state: "Diasone has proved to be effective in the treatment of leprosy in a series of 42 patients observed for 8 months." Braza, Diniz, Lima and Schuyman of Brazil;<sup>12</sup> Mom of Costa Rica;<sup>12</sup> Wharton of British Guiana;<sup>12</sup> Castello of Cuba<sup>13</sup> and Sloan of Hawaii<sup>14</sup> have all reported favorably. At the Second Pan American Leprosy Conference held in Rio de Janeiro, Brazil, in October 1946, the Subcommittee on Therapeutics recognized the sulfone drugs as having an efficient therapeutic action in lepromatous leprosy although the committee felt it was too early as yet to approve them as definite chemotherapeutic agents for the disease.<sup>15</sup>

#### CHEMICAL STRUCTURE

Promin, diasone, and promizole are related chemically to one another by having in common the diamino diphenyl sulfone radical. There is reason to believe that the diamino diphenyl sulfone radical is the active principle. This belief, however, has not been definitely established. Sulfone derivatives while similar in chemical composition to sulfa or sulfonamide drugs should not be confused with the latter. The parent radical in the former drugs is a double benzene ring structure as distinguished from the single benzene ring structure present in the parent radical of the sulfa or sulfonamide series of drugs. This difference in chemical structure might well account for the difference in toxicity exhibited between these two classes of drugs as well as therapeutic activity.

#### TOXIC MANIFESTATIONS

Sulfone drugs are comparatively free from any severe toxic effects. Promizole is the least toxic of them all. The most fre-



quent toxic effect encountered is a slow destruction of erythrocytes. Infrequently, leucopenia and allergic dermatitis occur. Nausea, vomiting, lack of appetite or headaches are seldom encountered and never severe. These latter symptoms are most frequently seen in the orally administered drugs, although nausea and vomiting and sometimes sneezing may be seen immediately after intravenous injection of promin. Hematuria or crystaluria has not been seen in our group of patients except early in the experience with diasone. When treatment was first initiated patients were given maximum dosages from the start. Hematuria without crystaluria occurred in some patients. When treatment was begun with small doses of the drug and gradually increased over a period of weeks as tolerance was increased, no further difficulty occurred.

To guard against any toxicity which might occur certain precautions are practiced in the treatment regime that has been established. Dosage is kept low at the beginning of treatment and gradually increased as individual tolerance is gained. Thus, the dosage of promin ranges from 1.0 gram to 5.0 grams daily, that of diasone from .3 gram to 1.0 grams daily, and that of promizole from 1.0 gram to 8.0 grams daily. Rest periods are also provided every third week for patients treated with promin and for a period of 2 weeks every 2 months for patients taking diasone and promizole. During the rest periods the patients' hematopoietic system is usually afforded time to restore the blood cells lost through the hemolytic action of the drug. Occasionally, it is necessary to administer iron and liver extract as adjuvants for anemia. Urinalysis, red and white blood counts, and hemoglobin estimations on each patient every three weeks, and frequent clinical examinations are performed in order to detect manifestations of toxicity early.

#### INTENSIVE PROMIN THERAPY

Sulfone drugs are rapidly eliminated in the urine. Only traces of the drugs remain in the blood stream 24 hours after administration. Six to eight hours after the in-

travenous injection of a 5.0 gram dose of promin only a relatively small amount remains in the blood stream. Recently, therefore, a small group of patients have received a 5.0 gram dose of promin intravenously three times daily in order to determine whether or not the therapeutic response will be more rapid when the promin blood level is held high. Results to date would indicate that there is an accelerated response but it is still not determined whether or not the therapeutic response is sufficiently accelerated to justify the added risk and added administrative procedure involved.

#### THERAPEUTIC EFFECTS

While only objective improvement as demonstrated by frequent clinical examinations, photographs, and laboratory evidence have been considered in evaluating the therapeutic effects of the sulfones, the marked subjective improvement after treatment with these drugs cannot be overlooked. Both types of improvement are slow in coming. Definite objective improvement, as a rule, seldom becomes manifested before 6 months of treatment. After this, improvement is progressive with few if any relapses.

Mucous membrane lesions usually are the first to respond to treatment. Oral and laryngeal nodules, ulcers, and infiltrations usually subside and disappear after a few months treatment. The patient's voice is restored and dyspnea is relieved. Emergency tracheotomies become unnecessary. Nasal obstruction and epistaxis are relieved through the healing of inflammatory mucosal lesions.

Improvement in skin lesions follows. Nodular lesions slowly shrink and flatten. If the lesions originally were large and deepseated they disintegrate more slowly and heal with subsequent scar formation. If small they are completely absorbed leaving only a pigmented spot. Infiltrative plaques gradually subside with diminution of inflammatory swelling and edema of dermal tissues. At times, the infiltrated part of the skin assumes a greyish to purplish hue as it undergoes healing.

Leprous ulcers of the extremities gradually become disinfected and form healthy granulations and heal through scar formation. Trophic plantar ulcers, unless the trophic disturbance is exceedingly severe, granulate and gradually close with residual callosities. Occasionally, regrowth of hair occurs in eyebrows, beard and arms and legs.

Leprous eye lesions seem capable of offering a considerable degree of resistance to sulfone therapy. Although, in general, the progress of conjunctival, corneal and iridocyclitic leprosy infiltrations is checked and there is occasional improvement in impaired vision, stubborn attacks of repeated severe acute iridocyclitis in some patients do occur while treatment is in progress. This is especially true when the eye conditions are of long standing. It would appear from our experience in this field that here early treatment is of utmost importance.

Another example of the slow action of the sulfones is seen in the resistance offered by *M. leprae* as demonstrated by skin and nasal smears. During the first year of treatment practically all lepromatous cases remain bacilliferous. During subsequent years of treatment, an ever increasing proportion of patients revert from positive to negative. It is possible, therefore, to secure an arrest of the disease,<sup>16</sup> and the return of the patient to his home. Early cases appear to respond faster in this regard than cases of long standing. So far, no relapses of arrested cases have been reported.

Many patients while improved remarkably from the clinical standpoint continue to be positive bacterioscopically after several years of sulfone therapy. This slow disappearance of the organisms from the lesions would indicate that sulfones have little if any destructive effect upon the acid-fast organism in the tissue cells. Fite<sup>17</sup> in his study of the histopathology of lesions before and after promin treatment found that promin appears capable of eliminating bacillary infection from the blood stream and small blood vessels thereby preventing the formation of new lesions. The lesions

already present are then afforded a better opportunity to recede much as they would recede during spontaneous regression.

Attacks of acute lepra reactions with erythema nodosum or erysipeloid dermatitis are not commonly aborted by sulfone therapy. Patients experiencing such episodes previously may have recurrence during the course of treatment. However, severe lepra reactions are not nearly as frequent as formerly but there is some evidence to indicate that the mild, more or less evanescent, attacks of erythema nodosum might be, at times, precipitated by the sulfone drugs. Episodes of acute leprosy neuritis are also not prevented or aborted. Severe attacks of neuritis occur quite frequently. Following such acute nerve reactions, loss of sensation, muscle atrophy, paralysis and contractures occur occasionally, in spite of treatment. On the other hand, many patients not suffering from acute nerve reactions have partial return of sensation over anesthetic areas as treatment progresses. This is probably due to a mechanical release of pressure resulting from reduction of the pathological changes along the nerve trunk rather than to a regrowth of axis fibers.

Subjective improvement as previously stated occurs concurrently with objective improvement. In addition to the relief of nasal obstruction, hoarseness, and dyspnea, patients develop a sense of well being. They have more pep, sleep better and, in general, feel as if they have a new lease on life. Weight gain is universal; in fact, some patients must be cautioned against gaining too much weight.

#### DISCUSSION

Although definitely not a cure all, the sulfone drugs have proved therapeutically more effective in lepromatous leprosy than any previous treatment tried at Carville. No claim, however, is made that these drugs are specific remedies for leprosy. The superiority of the sulfones over chaulmoogra oil is significantly demonstrated at Carville by the complete abandonment of the latter treatment for the routine treatment of leprosy in favor of the sulfones.



Final conclusions as to the efficacy of the sulfones, however, cannot as yet be given. It is possible that leprosy cases treated with the sulfones might reactivate as cases treated with chaulmoogra oil have. So far no relapses have occurred, but it is yet too early to say that none will.

The mode of action remains unknown. The drugs appear to prevent the formation of new lesions. In doing so they allow the body defenses to deal more effectively with the old lesions which seem to disappear by simple atrophy.

Residual deformities of hands, feet, face, and eyes as seen in far-advanced cases of the disease, naturally, are not reversible. Consequently, it is evident that early treatment in leprosy is as necessary as in cancer, tuberculosis or syphilis in order to secure the best results—and possibly prevent such deformities from occurring. Early treatment requires early diagnosis. Since an effective remedy is in their hands, all physicians, especially those in the states where leprosy is endemic, should increase their index of suspicion for this age old disease as they have for cancer, tuberculosis, and syphilis so that cases of leprosy also might be found and placed under treatment early.

#### CONCLUSIONS

(1) The sulfone drugs, promin, diasone, and promizole have been found to be effective remedies for leprosy.

(2) Although no claim is made that they are specific remedies, objective and subjective clinical improvements are produced by these drugs that cannot be attributed to spontaneous regression of the disease.

(3) Improvements are slow in their development but are progressive during the course of treatment. The disease, seldom if ever, appears to get worse while under treatment.

(4) Laboratory examinations indicate a

slow but steady decrease in acid-fast organisms in the skin. Negative skin smears and arrest of the disease occur. So far no relapses of arrested cases have been reported.

(5) Early treatment of leprosy cases through early diagnosis is a goal to be achieved.

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#### CORRECTION

In the first line of paragraph five of Summary and Conclusion on page 427 of the paper entitled "A Review of Certain Aspects of the Pathologic Physiology of Heart Disease" by Roderick C. Webb, M. D., the third word should be "left-sided" instead of "rightsided."

# NEW ORLEANS Medical and Surgical Journal

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## HORMONE THERAPY IN MAMMARY CANCER

The effect of various hormones on carcinoma of certain organs is a subject continually before physicians in many fields. The palliative treatment of inoperable carcinoma of the breast with metastases, by the use of estrogens and androgens is a matter of present interest. It is agreed by observers that the only prospects of cure come from surgery and/or radiation in the manner currently used. The helpfulness of hormone

therapy is limited in its possible palliative effect in metastatic carcinoma. A summary of observations to date is made by the Council on Pharmacy and Chemistry of the A.M.A.<sup>1</sup> It is felt that vigorous androgen or estrogen therapy should be undertaken with caution and with a knowledge of its limitations.

The possible usefulness of the androgens seems to be in the field of bone metastasis. Testosterone propionate, by needle, 100 mg. three times a week for ten weeks is suggested. This is followed by 60 mg. methyl testosterone a day by mouth for ten weeks. The benefits are similar to those seen in prostatic carcinoma after castration. Scant relief is to be expected in metastatic lesions in the soft tissues.

Estrogen therapy has been followed by regression in the primary tumors and soft tissue recurrences. It appears that it had best be used in patients about 60 years of age and over. Care must be used in elderly patients with cardiac disease as decompensation may be precipitated as a result of retention of fluid.

The following additional warnings are given:

"Because of the inherent dangers of indiscriminate steroid therapy of mammary cancer, the experimental nature of this therapy must be emphasized. The Subcommittee believes it imperative to reemphasize the known dangers and to point out that others may be discovered in the investigations now contemplated. The known dangers are reiterated:

**"Androgen Therapy.**—In cases of metastatic bone lesions with high blood calcium levels (such, for example, as 14 mg. per hundred cubic centimeters or above) certain patients have been made extremely ill, having nausea, vomiting and prostration, by the instigation of testosterone therapy. It is necessary to determine the blood calcium level on each patient before commencing testosterone therapy and, if the calcium level is high, during the course of treatment.

**"Estrogen Therapy.**—Any patient who still menstruates or who has menstruated



within a five year period should definitely not receive estrogen therapy, as it accelerates the rate of growth of the carcinoma.

"Large therapeutic doses of estrogen eventually produce uterine bleeding; it then becomes necessary, temporarily at least, to diminish the dosage.

*"Androgen and Estrogen Therapy.*—Androgen and estrogen therapy should never take the place of radical surgery in operable mammary carcinoma."

1. JAMA 135:987 (Dec. 13) 1947.

## ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

***An informed profession should be a wise one.***

### REPORT OF THE PRESIDENT OF THE LOUISIANA STATE MEDICAL SOCIETY

The year 1947 was indeed one of soul trying trials and tribulations for the officers of the Louisiana State Medical Society who were beset and bedeviled from many sides; nevertheless the year can, on the whole, be regarded as very successful and rich in accomplishments.

Meetings were attended in each district of the state. The scientific programs were, in general, well prepared and in some instances outstanding in merit. Attendance figures were surprisingly good on a few occasions but disappointing in about as many. The affairs of the State Society provoked lively interest in a few members in every district but such interest was more than offset by ignorance, apathy or indifference on the part of a far greater number. An officer of the Society must, of necessity, be disturbed by the number of members who are not only completely ignorant of what the Society is doing but seemingly are additionally complacently indifferent. While we were frequently asked "What do you do with the money?" or "What do we get for our dues?" there was no real discontent or bitter criticism and we are happy to report we encountered no internal strife or serious discord.

It is with extreme distress that I report death in our official family during the year. We lost Dr. John T. O'Ferrall, who was

Councilor of the Second Congressional District and who for years had been interested and active in organized medicine. His place will be difficult to fill in our ranks, both professionally and personally.

After some twenty years of faithful service, we also lost during the past year Dr. John Herr Musser, Editor of our Journal. The membership of the State Society is joined by a host of other individuals and organizations in mourning his passing. We deemed ourselves fortunate indeed in being able to obtain the services of Dr. Philip H. Jones for the post of Editor. Dr. Jones needs no introduction to this Society but I bespeak for him your hearty support and cooperation.

Dr. Joseph A. O'Hara, a Past President of the Society, also died during the past year and his passing was a serious loss to his community and to organized medicine.

#### INSURANCE

During the past year the United States Fidelity and Guaranty Insurance Company, with whom we had carried a master policy with individual membership against malpractice suits, canceled their contract. We were fortunate and happy to make immediate arrangements for writing a new contract with the Aetna Casualty and Surety Company which has carried protection for the Orleans Parish Medical Society for a number of years as well as for many other similar groups throughout the Country.

## SOCIALIZED MEDICINE

Although the bills for government socialization of medicine were not reported out of the committees a very active fight was carried on throughout the entire year and a serious warning must be sounded against any relaxation of vigor or any sense of security or complacency in this fight which is being waged relentlessly and constantly by those whom we consider enemies of organized medicine. We need to recall only the President's message to realize the ever-present danger. The Louisiana State Medical Society has participated actively in combatting these bills and in comparison with many other states we believe we can say with justice we have actually done more than our share. There is no doubt that this fight is going to be a long drawn out one and attention might be called to the recent events in England in this connection and the experience of the doctors of San Francisco with a large municipal service organization. We are not only threatened by governmental medicine in many different guises but also by the gradual assumption of the practice of medicine or at least the management thereof, by various lay groups as they become larger and more powerful. This tendency has been very evident on many sides and an example may be cited in the recent organization of a society for the purpose of combatting a national organization in the management of blood collection, transfusion and so forth.

## SOUTHERN REGIONAL CONFERENCE

The Southern Regional Conference of the American Medical Association, representing seven states, was held in New Orleans in October. The Society cooperated in this meeting and received very cordial letters of thanks and appreciation from the officers of the AMA, who considered it the most successful meeting of this type.

## COUNCIL ON MEDICAL SERVICE AND PUBLIC RELATIONS

The Council on Medical Service and Public Relations has not only been very active during the past year but has planned an ambitious and far-reaching program for the coming year. They are fighting vigorously socialization and regimentation of

medicine and deserve our unqualified support. Funds are needed for this fight and I urge that they be granted. I believe the annual dues collected from the members of the Louisiana State Medical Society should be spent for the benefit of the men who pay the dues and not saved and invested in government bonds. I believe that, except for a reasonable sum set aside for unforeseen emergencies, the monies should be spent as collected for the good of the Society, for I can see no reason for accumulating large savings. I recommend that the House of Delegates approve, in principle, such a plan for the guidance of the Budget and Finance Committee.

## COMMITTEE ON RURAL MEDICAL SERVICE

The Committee on Rural Medical Service has likewise been very active and has done splendid work during the past year and they need our continued support and encouragement. The general purposes, work, and fields of endeavor of this Committee and the Council on Medical Service and Public Relations, are so closely inter-related that it is suggested that a plan be formulated by which they may be combined into one committee or at least a much closer affiliation and integration arranged. It is also deemed advisable, in this connection, that serious consideration be given the employment of a competent secretary for work in these fields as such a man could be used very well to the advantage of organized medicine in general and possibly might also function as an assistant in the office of the Secretary-Treasurer, Dr. Talbot.

## LOUISIANA PHYSICIANS SERVICE, INC.

The Louisiana Physicians Service, Inc. has encountered the troubles and disappointments which we have learned are experienced by every such plan in its first year or two. At one time the whole structure seemed precarious but certain adjustments were effected which eased the acute strain. The Executive Committee of the State Society requested a committee of six nationally prominent and recognized authorities in the fields of prepaid medical care and hospital insurance to come to Louisiana and make a study of the manage-



ment and closer cooperation and coordination between LPS and the Blue Cross organizations. The Blue Cross organizations readily agreed to cooperate in the survey. The report of this committee was very helpful and practically all of their recommendations have been acted upon. These gentlemen very graciously gave of their time and service at no cost whatsoever to the State Society. Our experience has shown us clearly that we need the advice and counsel of practical business men in the management of LPS and the above mentioned committee included such a recommendation. In order that lay members may be chosen in an orderly and managed fashion, a panel of some twelve names should be set up each year by the State Society from which list of names the LPS must select its lay directors; this should follow practically the same plan by which the medical members of the Board of Directors of LPS are chosen. The Board of Directors should be increased to 15, of whom no more than four may be lay members.

#### SECRETARY-TREASURER

The House of Delegates, the Executive Committee, and the Society in general, are all well aware of the capability, devotion and sincerity of our Secretary-Treasurer, Dr. P. T. Talbot. The daily load of work in his office is constantly increasing and becoming more burdensome. Dr. Talbot's salary was fixed many years ago and has never been increased. In the meantime prices of all necessities have spiraled to unbelievable heights and what was once an adequate salary may now be decidedly otherwise. It is my opinion that Dr. Talbot has earned, deserves, and should have an increase in salary, quite regardless of the present economic pressure which makes such an increase an urgent necessity.

Because of the rapidly increasing burden of work in this office it is recommended that serious consideration be given employment of a younger man to act as an assistant to Dr. Talbot and who might, of course at the same time, be familiarizing himself with the work and detail of the office

against such time as Dr. Talbot may desire to retire. It is my opinion that a Doctor of Medicine should be chosen for this position because our experience indicates that the profession will be understood in a more sympathetic and comprehensive manner by one who is himself a doctor and can therefore appreciate from the standpoint of a physician rather than that of a business manager or executive such problems as may arise from time to time. It might, of course, be possible for the office of the Secretary, the Council on Medical Service and Public Relations, and the Committee on Rural Medical Service, to prorate among themselves this person's time so that he could function in such a dual capacity.

#### CONCLUSIONS

I desire to express my sincere and heartfelt thanks to the Society at various levels; first to the Society as a whole for conferring upon me the outstanding honor of selecting me as President; to the committees, from the Executive Committee, right down the line—not only has no committee ever shown any reluctance to cooperate to the fullest or carry out any request or suggestion but they have on the whole been alert and active and some of them, particularly the Council on Medical Service and Public Relations, Rural Medical Service Committee and Committee on Congressional Matters, have done outstanding work. I want to thank the officers of the component societies for their excellent meetings and invitations to same and finally those individual members whose names are legion upon whom I called for help, encouragement and assistance during the year. Whatsoever I asked was always promptly forthcoming and I can wish my successor nothing better than I had along these lines. Through the year Paul Talbot has stood "like a great rock in a weary land." This gentle, kindly man is both a tower of strength and a well of wisdom and understanding and without his constant presence at my side as guide, philosopher and friend the burden of the presidency would have

indeed been heavy. I thank him sincerely. Recognition and thanks must be given Miss Annie Mae Shoemaker for her efficient management and cheerful manner and also

to other personnel in the office who have been of assistance.

GILBERT C. ANDERSON, M. D.,  
President.

## LOUISIANA STATE MEDICAL SOCIETY NEWS

### C A L E N D A R

#### PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

#### NEW BOOKLET DESCRIBES SERVICES OF STATE SOCIETY

"Services of Your State Medical Society" is the title of the new booklet prepared by the Council on Medical Service and Public Relations of the Louisiana State Medical Society and recently mailed to every member of the State Society.

The booklet tells of the services offered by your State Medical Society; tells briefly of the basic organization of the Society and also explains what the Louisiana State Medical Society is, giving a brief history and construction of the operations of the organization.

The services are divided into three parts and explanation is given concerning the principal activities of the Society, the services furnished on a personal basis, and also tells what doctors can do to help their State Society.

Included in the booklet is a drawing showing the physical structure of the Society from the physician down to the functioning committees.

It is suggested that each doctor take time out to review this booklet and apprise himself of the activities of organized medicine and what it is doing today in his behalf.

#### THIRD DISTRICT MEDICAL SOCIETY

At a meeting of the Third District Medical Society held at the Lafayette Charity Hospital, Lafayette, on January 22, the following officers were elected: Dr. L. M. Villien, Jeanerette, President; Dr. S. D. Yongue, Breaux Bridge, Vice-President; Dr. I. W. Gajan, Jr., New Iberia, Secretary-Treasurer. Dr. F. H. Davis, Lafayette, was elected delegate to the State Society Meeting and Dr. H. M. Flory, New Iberia, was elected alternate. An excellent scientific program consisting of a paper by Dr. Sidney Chipman on "Infantile Croup" and a

paper on "Use and Abuse of Forceps" by Dr. Curtis Lund, were presented. This organization has recently been reactivated following a wartime furlough and the new officers are anxious to have a representative organization. All doctors of the district are therefore asked to pay their dues for 1948 to the secretary-treasurer now.

A unique type of postgraduate education is being offered through the Third District Medical Society. The course, given by seven prominent physicians and dentists from the University of Illinois started on Wednesday, March 31 and will be given for a period of six consecutive weeks from 7:30 to 9:30 p. m. on Wednesday evenings. The course is expected to be of value not only to the physician in general practice but also to the oral and maxillofacial surgeon and the otolaryngologist. The American Cancer Society is covering the cost of this course. The unusual feature about the program is that it can be heard without going to Chicago. It is presented in New Iberia in the Frederic Hotel Gold Room through the facilities of amplified long distance telephone communication and is illustrated by slides and movies sent there for the purpose. This is only the second time this method has been used in the world for the purpose of bringing scientific meetings to the doctor instead of the doctor going to the meetings. The first trial, in Scranton, Pennsylvania, was very successful. This series of lectures will present the subject of "Oral Cancer" in all of its aspects. Due to the present aroused public interest in cancer physicians are urged to attend as many sessions as possible.

#### IBERIA PARISH MEDICAL SOCIETY

A dinner meeting of the Iberia Parish Medical Society was held on February 5 at which time the following officers were elected: Dr. I. W. Gajan,



Jr., New Iberia, President; Dr. D. E. Bourgeois, New Iberia, Vice-President; Dr. Leon Slipakoff, New Iberia, Secretary-Treasurer. It is planned to hold quarterly scientific meetings of this organization.

#### EAST AND WEST FELICIANA BI-PARISH MEDICAL SOCIETY

The East and West Feliciana Bi-Parish Medical Society was entertained by Dr. Glenn J. Smith and the staff of the East Louisiana State Hospital in Jackson on March 3. After an excellent dinner a scientific program at which Dr. J. W. Dowell, of Baton Rouge and Dr. Wirth Wilkinson, of Jackson, presented excellent papers, was held. Vote of thanks was extended Dr. Smith and the staff of the hospital for their excellent entertainment and to Drs. Dowell and Wilkinson for their participation in the program. Drs. Dowell and Hamilton were elected members of the organization. The next meeting will be held on the first Wednesday in June.

#### NEWS ITEM

Dr. Rene J. Dubos, Professor of Comparative Pathology and of Tropical Medicine at the Harvard Medical School presented results of his researches on tuberculosis together with plans for future operations, in connection with the Sigma XI National Lectureships, on April 8 at 8 p. m. in the auditorium of Hutchinson Memorial Building.

#### PUBLIC RELATIONS PROGRAM EXPLAINED TO THREE PARISH MEDICAL SOCIETIES

The Public Relations Program of the Council on Medical Service and Public Relations of the Louisiana State Medical Society has been presented to three parish medical societies within the last month.

The Public Relations Program was presented to the Avoyelles Parish Medical Society at a meeting held in Marksville on Friday, February 27, at the Avoyelles Country Club. Dr. A. V. Friedrichs, Chairman of the Council on Medical Service and Public Relations, explained the public relations program in detail. Mr. Frank Lais, Jr., executive Director of the Council, briefly described some of the details of the program.

Dr. O. B. Owens, a member of the Council and President of Louisiana Physicians Service, explained the operations of Louisiana Physicians Service, the BLUE SHIELD plan which is the surgical and obstetrical care plan sponsored by the State Medical Society.

Dr. D. B. Barber, President of Louisiana Hospital Service, a Blue Cross plan, explained the benefits of Blue Cross Hospital Service.

Dr. P. T. Talbot, Secretary-Treasurer of the Louisiana State Medical Society, explained the functions of the State Medical Society.

The second presentation of the Public Relations

Program to a parish medical society was made by Frank Lais, Jr., Executive Director of the Council, to the East Baton Rouge Parish Medical Society on Tuesday, March 9. Mr. Lais explained to the members of the East Baton Rouge Parish Medical Society the complete Public Relations Program as presented by the Council on Medical Service and Public Relations and emphasized the necessity for active participation in the program by every doctor in the state.

The third presentation of the general Public Relations Program was made to members of the Lafourche Parish Medical Society and its Woman's Auxiliary at a joint meeting held in the home of Dr. Guy R. Jones in Lockport on Monday, March 15. Dr. Jones is Chairman of the Committee on Rural Medical Service and many of the objectives of the Public Relations Program include a joint presentation of the activities of the Council on Medical Service and Public Relations and the Committee on Rural Medical Service.

Mr. Lais presented the Public Relations Program and Mrs. T. R. Tomlinson, Chairman of the Louisiana Rural Health Council, explained the activities of the State Health Council in organizing parish health councils. The parish health councils are being organized under the leadership of the Council on Medical Service and Public Relations of the Louisiana State Medical Society and the Louisiana Farm Bureau Federation, together with other voluntary agencies interested in health.

#### COUNCIL ANNOUNCES SEVEN ACTIVE RADIO PROGRAMS

Seven active radio broadcasts are being presented throughout Louisiana and three additional broadcasts have been tentatively arranged for the presentation of the AMA transcribed health series which are loaned to the State Medical Society for reproduction. Active programs are being presented over the following radio stations on the day and time designated:

KNOE—Monroe—"BEFORE THE DOCTOR COMES"—Every Wednesday, 1:30 p. m.

KTBS—Shreveport—"THE STORY OF SURGERY"—Every Saturday, 4:00 p. m.

KWCJ—Natchitoches—"KEEPING YOUR BABY WELL"—Every Monday, 3:30 p. m.

KRUS—Ruston—"KEEPING YOUR BABY WELL"—Every Thursday, 2:45 p. m.

WJBO—Baton Rouge—"THAT WONDERFUL FEELING"—Every Tuesday, 10:45 a. m.

WIKK—Bogalusa—"DODGING CONTAGIOUS DISEASES"—Every Sunday, 12:45 p. m.

KCIL—Houma—"MORE LIFE FOR YOU"—Every Saturday, 9:15 a. m.

These broadcasts are presented by the Council on Medical Service and Public Relations of the Louisiana State Medical Society in cooperation with the individual parish medical society in the area where the radio station is located.

The series being presented are educational in scope and it is the desire of the Council on Medical Service and Public Relations that each doctor inform his patients of these broadcasts and encourage the patients and their families to listen to them. It is only through cooperation of the doctors and their efforts in calling these programs to the attention of their patients that they can successfully be reproduced.

#### AMERICAN MEDICAL ASSOCIATION SAYS PUBLIC DEMAND FOR SERVICE AT NIGHT MUST BE MET

The American Medical Association calls on county medical societies to meet the public demand for emergency medical service at night.

"From many sections of the United States," says an editorial in a recent (March 6) issue of *The Journal of The American Medical Association*, "complaints have come lately that persons who have called physicians late at night have been unable to secure attendance from either those whom they considered their family physicians or from specialists or, indeed, from any physician."

The American Medical Association says that large county medical societies or urban groups should maintain a physicians' telephone exchange which would take the responsibility for locating physicians if response is not made to the ringing of the telephone in the home or in the office.

The solution is simple and practical, requiring only a minimum of community organization. A number of county medical societies already maintain a physicians' telephone exchange where doctors' calls may be received and doctors located if their office or home telephones do not respond. Such an exchange can be utilized at night or on holidays, simply by furnishing the exchange with a list of physicians who are able and willing to make night calls. Such physicians would probably include the younger general practitioners, newcomers to the community, and others in general practice. If such a roster were available, and its availability widely publicized, night calls for medical service would soon gravitate to this center and the patient would be assured the services of a physician.

Under such a system the necessity for calling many doctors would be eliminated. Two calls at most would be necessary. Where there is no physicians' telephone service, it might be possible to have the hospitals cooperate by handling such night calls.

The Medical Society of the District of Columbia and the Milwaukee County Medical Society have found such a plan practical, as have a number of other societies.

By this simple and practical expedient, which is doubtless in effect in modified form in a number

of communities, the sick can be served and the medical profession can redeem its pledge of unselfish public service.

It is highly important that where such arrangements exist they be brought to the attention of the lay people in the community through appropriate public channels, not once but repeatedly, to keep the shifting populations well informed.

Few problems in the field of medical service have aroused so much public discussion. Whether resentment against physicians is justified or not, it does harm. The solution for this problem is so eminently simple and would reflect so favorably upon physician-patient relationships that medical societies everywhere are urged to give it serious consideration immediately.

#### EXAMINATIONS FOR APPOINTMENT OF MEDICAL SCHOOL GRADUATES IN NAVY MEDICAL CORPS

Examinations for the selection of candidates for appointment to the grade of Lieutenant (Junior Grade) in the Medical Corps of the Navy will be held at Naval hospitals in continental United States during the period May 3-7.

Graduates of approved medical schools in the United States or Canada who have completed intern training in accredited hospitals or who will complete such training within four months of the date of the examination, and who are physically and otherwise qualified, are eligible to take the examination.

Candidates, who must be less than 32 years of age at the time of appointment, will be required to appear before boards of medical examiners and supervisory Naval examining boards at the Naval Hospital nearest their place of residence to demonstrate their physical and professional qualifications for appointment.

Following approval by the President of the United States, selected candidates will receive their appointment and orders assigning them to duty in a Naval medical facility for active Naval service.

Public law 365 of the Eightieth Congress, approved August 5, 1947, provides additional compensation at the rate of \$100.00 a month for each month of active service performed by Medical Corps officers of the Navy. This is in addition to any pay, allowances or emoluments that Medical Corps officers are otherwise entitled to receive, and by the provisions of the law, the amount paid to any one officer under this authority is limited to a total of \$36,000 computed on the basis of \$1,200 yearly over a period of 30 years active service.

Detailed information concerning the form and procedure of application may be obtained from Naval Officer Procurement Offices or from the Bureau of Medicine and Surgery, Navy Department, Washington, D. C.



### SCHOLARS IN MEDICAL SCIENCE SELECTED BY MARKLE FOUNDATION

Sixteen young scientists have been appointed as the first group of Scholars in Medical Science, under the plan announced last fall by the John and Mary R. Markle Foundation to support qualified young scientists who wish to make a career in academic medicine. The Scholars were selected from candidates nominated by accredited medical schools in the United States and Canada by regional committees appointed by the Foundation. Toward the support of the Scholars and their research the Foundation has allocated a total of \$400,000 to their respective medical schools, each school to receive \$25,000 payable at the rate of \$5,000 annually for five years.

As faculty members of the participating medical schools, the Scholars will devote the next five years to teaching and research, at the end of which time they will have had an opportunity to become established teachers and investigators. According to John M. Russell, Executive Director of the Foundation, an undetermined number of Scholars will be appointed each year for the next few years for the long-range purpose of strengthening the faculties of medical schools, and medical education generally.

### BLUE SHIELD ADOPTED NATIONALLY

BLUE SHIELD has been adopted as the official name and insignia for the non-profit, prepayment medical care plans in the United States, as the result of action taken recently by the Commission of Associated Medical Care Plans.

Prior to the establishment of AMCP in 1946, several medically sponsored prepayment plans had begun to use a BLUE SHIELD symbol on their literature, one of which was Louisiana Physicians Service, the practice having originated in 1939 with Western New York Medical Plan in Buffalo, New York.

Having secured permission from eighteen plans already utilizing the insignia, the AMCP Commission adopted BLUE SHIELD as the official service mark for its forty-eight member plans.

It is anticipated that BLUE SHIELD will gain widespread public acceptance, identifying the prepayment programs sponsored by the medical profession.

The BLUE SHIELD plan serving the State of Louisiana is known as Louisiana Physicians Service and is sponsored by the Louisiana State Medical Society, with its home office in New Orleans. The plan cooperates with Blue Cross in Baton Rouge, Alexandria, Shreveport, and Monroe.

The adoption of BLUE SHIELD will not replace the Seal of Acceptance of the AMA, awarded by the Council on Medical Service to prepayment plans which have complied with established minimum standards.

The easiest way to distinguish the Blue Shield

symbol from that of the AMA is to remember that the Seal of Acceptance, granted by the AMA Council on Medical Service, indicates AMA approval. BLUE SHIELD is a promotional device, adopted by AMCP and its member plans, all of whom follow the non-profit principle of operation.

Whether referred to over the radio, in advertising copy, or news releases, BLUE SHIELD provides an easily recognizable verbal and visual means of identifying the nation's non-profit plans for prepaying the costs of medical care.

On January 1, 1948 the non-profit plans recorded a total enrollment in excess of 7,000,000 persons.

### PUBLICATION ON INFANTILE PARALYSIS

The 1948 edition of "Facts and Figures about Infantile Paralysis," a publication of the National Foundation for Infantile Paralysis, is now available to physicians and public health workers. Statistics on the disease, revised yearly, are gathered from the United States Public Health Service, state health departments and various other sources.

Incidence of infantile paralysis in the United States is shown in tables, maps and charts. Other statistics furnish information on age and sex distribution, case rates, crippling conditions and mortality. For the first time, this publication includes data on the disease in foreign countries.

Copies of the booklet (No. 59) may be secured free of charge by writing Education Service, The National Foundation for Infantile Paralysis, 120 Broadway, New York 5, N. Y.

### NEW ORLEANS DISTRICT OF L. S. U. MEDICAL ALUMNI ASSOCIATION

At a meeting held at the L. S. U. School of Medicine on March 18 the New Orleans District of the L. S. U. Medical Alumni Association was organized. Approximately 75 of over 350 alumni practicing in New Orleans were present to hear Dean Vernon Lippard discuss the changes which have been made in the staff and plans for future expansion of the school. Following his address Dr. Jack R. Anderson was elected president of the district alumni association, Dr. Elliot Roy, vice-president and Dr. Philip Cenac, secretary-treasurer. Meetings will be held quarterly and will be of a business-social nature. Data concerning each meeting will be published in the Bulletin of the Orleans Parish Medical Society and in the New Orleans Medical and Surgical Journal.

### AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC.

The general oral and pathology examinations (Part II) for candidates will be conducted by the American Board of Obstetrics and Gynecology, Inc. in Washington, D. C. May 16-22. The Shoreham Hotel will be headquarters for the Board and formal notice of the exact time of each candidate's examination will be sent him several weeks in ad-

vance of the examination dates. Hotel reservations may be made by writing direct to the Shoreham Hotel. Candidates for re-examination in Part II must make written application to the Secretary's office not later than April 1. Candidates in military or Naval Service are requested to keep the Secretary's office informed of any change in address. Applications are now being received for the 1949 examinations. For further information and application blanks address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

#### IN MEMORIAM

At a recent meeting of the Ouachita Parish Medical Society, held in Monroe, memorial services were held for the following members of the organization who died during the year 1947: Drs. F. C. Bennett, George M. Trezevant, David I. Hirsch, Ellis Powell and Leonard L. Shlenker. Appropriate resolutions were prepared and spread on the minutes of this meeting.

#### CHARLES CAMILLE DeGRAVELLES

1883 - 1948

Dr. Charles Camille DeGravelles, of New Iberia, died on March 23. In his passing the physicians lose a good friend and an eminent colleague. Dr. DeGravelles was born in 1883 in St. Mary Parish, graduated from Tulane University School of Medicine in 1910. He was a member of the Southern Medical Association and a Fellow of the American College of Physicians. He was Councilor from his district for many years and was president of the State Society in 1943. War problems and the political pressure for state medicine made this period a difficult one and Dr. DeGravelles handled the problems with skill and determination. He presented the Society's case in the matter of the federal "Emergency Maternal and Infant Care" plan ably and was a zealous defender of the interest of the physician. The doctor died as he had said would be his preference; he officiated in the induction of a new citizen and then lay down to rest. The Society feels his loss.

#### WOMAN'S AUXILIARY

The semi-annual Board Meeting of the Woman's Auxiliary to the Louisiana State Medical Society was held at the Orleans Club on February 26, with Mrs. J. W. Warren presiding.

It was voted that a news letter be sent monthly to every member of the Woman's Auxiliary. This letter will be a very effective medium to advise the members of current events of the Auxiliary and instructive as to the various duties of its members.

Mrs. Warren introduced Mrs. Marquis C. Wiginton to the group as their Representative of the Auxiliary to the Rural Health Conference. Mrs. Wiginton is also serving on the Committee on Nursing with Mrs. Booker Wilkinson, Chairman, representing the Louisiana Federation of Women's Clubs. Mrs. Wiginton was highly complimented by Mrs. Warren on her work in connection with the Rural Health Conference. It is believed that with their coordinated efforts they can formulate a sound program by which medical and dental case might be improved not only in rural sections but throughout the whole country.

The Calcasieu Parish Auxiliary has been very active this past year. Their last year's project was the Doctors' Library, which was started on Doctors' Day by donations from members of their chapter. Mrs. L. Kushner, Chairman, is still collecting and labeling books.

In relation to the Preservation of Medical Cultural Items, the Calcasieu Auxiliary is collecting material on the duties and activities of their doctors who left the Parish for active military duty. This material will be compiled in a book and displayed in Lake Charles on Doctors' Day before sending it to New Orleans.

Another fine job of the Calcasieu Auxiliary is their organization and opening of a Cancer Control Clinic consisting of five doctors, two nurses, a pathologist, and a permanent secretary. This clinic was opened on February 2, and is sponsored by the Calcasieu Chapter of the Louisiana Division of the American Cancer Society.

## BOOK REVIEWS

*Medicine in the Changing Order*: Report of the New York Academy of Medicine, Committee on Medicine and the Changing Order, New York, The Commonwealth Fund, 1947. Pp. 240. Also, Introduction and Letter of Transmittal.

This book, a report of The Committee on Medicine and the Changing Order formed in 1942 by the New York Academy of Medicine, presents a factual study of the problem of providing adequate medical care throughout the country.

It is emphasized that the problem of providing adequate medical care is a complex one affording no simple solution and that the problem varies in different regions of the United States. In addition to purely medical aspects of the medical care problem—such as poor distribution of medical personnel, inadequacies of medical care facilities—the investigations of the Committee show that there is a close relationship between the social and economic conditions of an area and many of the diffi-



culties in providing adequate medical care.

According to the findings of the Committee, the problem of medical care emerges from the paradoxical situation that, as medical services have become more effective and desirable, they have also become more expensive and less generally distributed and, consequently, less available to many in need of medical attention. While admitting that medical care is better and more generally available in the United States to day than ever before, this report indicates that there is a definite need for improving medical care of many groups and for securing a more uniform distribution of medical services in many areas.

As a means of attack on this problem, government aid is favored along certain lines—such as increasing and improving public health services, subsidizing medical aid for indigent and low income groups, and assistance in the establishment and enlargement of hospitals. It is recommended that assistance from the government be administered locally insofar as practicable. This report further suggests that group practice of medicine, voluntary medical insurance, close cooperation among hospitals of all types, and greater attention to the practice of preventive medicine are other important means of solving the medical care problem. National compulsory medical insurance is looked upon with disfavor.

K. T. MOSLEY, M. D.

*Unipolar Lead Electrocardiography, Including Standard Leads, Unipolar Extremity Leads and Multiple Unipolar Precordial Leads:* By Emanuel Goldberger, B. S., M. D. Philadelphia, Lea & Febiger, 1947. Pp. 182. Price, \$4.00.

This monograph is the outcome of the author's study of unipolar leads and their relationship to standard leads and their clinical application.

He uses a central terminal that differs from the one first used by F. N. Wilson, in that ordinary electric wire minus the 5,000 ohms resistance is used. This central terminal is considered zero in potential. Therefore, when an exploring electrode is attached to a central terminal of this kind, the electrocardiogram is thought to represent the potential of the underlying region upon which this electrode is placed and is said to be unipolar. It is claimed that there is no difference in the curves made in this way and those made with the central terminal used by Wilson. This probably does not represent the opinion of all cardiologists.

Unipolar leads differ from the standard limb leads in that the latter are bi-polar and represent the difference in potential between the two limbs upon which the electrodes are applied.

The author for some time has used what he terms augmented unipolar extremity leads. These are made by breaking the connection between the central terminal and the limb on which the exploring electrode is placed. The form of the unipolar

extremity leads, the three standard leads, and the precordial leads depend on the position of the heart. Five basic unipolar lead patterns of the normal electrocardiogram are described. First—leads that face the epicardial surface of the left ventricle. Second—leads that face the epicardial surface of the right ventricle. Third—leads that face the cavity of the right ventricle. Fourth—leads that face the cavity of the left ventricle. Fifth—leads that face the back of the heart. The region of the chest where these patterns are usually found and the effect of the position of the heart and its rotation about its different axes are described and explained.

The author thinks it is necessary in every case to obtain the six unipolar precordial leads. They will show whether the basic ventricular pattern over the right and over the left ventricle are normal or not. The unipolar limb leads may show abnormalities in those regions of the heart that do not face the precordial leads. They also give valuable information about the position of the heart. In addition the three standard limb leads should be obtained.

The reviewer is of the opinion that this should be the minimum number of leads made in the vast majority of patients. It is sometimes necessary to go higher or lower on the chest, farther to the left and farther to the right to get the desired information.

There are numerous reproductions of electrocardiograms showing different heart conditions—myocardial injury, enlargement of the right and left ventricles, pericarditis, bundle branch block, digitalis effect, etc.—bringing out the changes in the electrocardiogram which are produced by the position of the heart and its rotation on its different axes.

The explanations and discussions in the text may not meet the approval of all, but do bring up some interesting points and will help one to understand some changes in the electrocardiogram produced by the rotation of the heart. There is quite a lot of repetition but this is probably an asset rather than a fault. There are about seven and a half pages of references. The reproductions with a few exceptions are nearly all good. To anyone interested in electrocardiography this small book should be helpful.

J. M. BAMBER, M. D.

*The Normal Encephalogram:* By Leo M. Davidoff, M. D., and Cornelius G. Dyke, M. D., 2d ed. Philadelphia, Lea & Febiger, 1946. Pp. 214. Price, \$5.00.

This is the second edition of a book that was written in response to the request of various specialists, neurosurgeons, neurologists, roentgenologists, pediatricians, and internists. It is the only book which fills the need for a presentation of the subject of pneumoencephalography.

Almost all of the illustrations are from the author's own series of 400 cases. Anatomical details are described and illustrated very clearly; there are 155 illustrations, and 214 pages. A discussion of the method and a history of the method of encephalography, and a complete bibliography, are found in this book.

WALKER THOMPSON, M. D.

*Obstetric Practice*: By Alfred C. Beck, M. D. 4th ed. Baltimore, Williams & Wilkins Co., 1947. Illus. Pp. 966. Price, \$7.00.

The fourth edition of Beck, printed in January 1947 is essentially the same as the third edition except for revision of the first chapter and the addition of a chapter on obstetrical analgesia and anesthesia. Minor revision compatible with advances in obstetrical thought are present but in the main the latest edition is almost page for page identical with the previous one.

Beck's *Obstetrical Practice* is noteworthy because of the profusion of illustrations which are welcome to both student and practitioner. It is concise, avoids as much as possible, academic discussions which are of little practical value and is at its best in the description and illustration of the mechanism of labor. It can be recommended as a ready reference manual for the student and general practitioner, although the specialist may find it a little less detailed than he might hope.

R. E. ROUGELOT, JR., M. D.

*Minor Surgery*: By Frederick Christopher. 6th ed. Philadelphia, W. B. Saunders Company, 1948. Pp. 1058. Price, \$12.00.

The sixth edition of Christopher's *Minor Surgery*, as the other editions have, will probably be of most value to the physician without complete formal training in surgery. For the general practitioner and the intern it fills a definite need. The subject matter is well organized and is readily available for quick reference and review. Extensive references are included with each chapter and cover material through 1946. Specific additions to the sixth edition include a section on thrombophlebitis and phlebothrombosis with consideration of femoral vein ligation in prophylaxis of pulmonary embolism and anticoagulant therapy. The use of antibiotics and sulfonamides is given proper emphasis.

Other new material includes gel foam and oxidized cellulose in the control of hemorrhage, early postoperative ambulation, procaine in serum sickness, lumbar sympathetic block in thrombophlebitis, intra-arterial penicillin in infections of the extremities, and the excision and closure of bed sores.

Direct quotation is used extensively by the author with good effect. Concise exposition of the small print quotations may be more widely read by the busy practitioner.

EVERETT H. CRAWFORD, M. D.

*Gifford's Text Book of Ophthalmology*: By F. H. Adler. 4th ed. Philadelphia, W. B. Saunders & Co., 1947. Pp. 512. Price. \$6.00.

The author of this fourth edition of Gifford's little classic in ophthalmology may not be known to some of our readers. He is high among this country's first five ophthalmologists, and our specialty is his debtor for this volume. His rare ability to simplify complex concepts will help many who are interested in ophthalmology to grasp more easily its fundamentals. The average reader does not realize the quantity and quality of blood, sweat, and tears that form the seasoning essential in making especially this type of book such a palatable and easily digested delicacy.

The chapters on visual and neuro-muscular functions and their disorders are presented with the clarity of a master. The table of contents, especially in medical works, illustrates the author's sense of sequence which is partly what makes medical classics, classics. In the chapter on the ocular manifestations of general diseases, the reviewer did not understand why metabolic and urinary diseases were placed between fungus and protozoal diseases. It is so much easier, however, to criticize the pécadillos of others than to do better ourselves that we critics are apt to develop a "holier than thou" complex, wearing self-constituted haloes which are too big for our heads and draping ourselves with mantles of Elijah which are really somewhat moth eaten.

The illustrations in this volume really illustrate which is more than can be said of those in most of the medical books which I have read and reviewed especially in these past several years. The judgment which the author has shown in the selection of current material and its presentation reflects his sound training and even sounder sense of medical values. Dr. Adler has created a truly beautiful and fitting memorial to the memory of our beloved friend and teacher, the late Dr. Sanford Gifford.

CHAS. A. BAHN, M. D.

#### PUBLICATIONS RECEIVED

Interscience Publishers, Inc., New York: *Physiology of Man in the Desert*, by E. F. Adolph, Ph. D. and Associates.

McGraw-Hill Book Company, Inc., New York: *Fatigue and Impairment in Man*, by S. Howard Bartley, Ph. D. and Eloise Chute, M. A.

The C. V. Mosby Company, St. Louis: *Psychobiology and Psychiatry* (2nd edition), by Wendell Muncie, M. D.

Charles C. Thomas, Springfield, Illinois: *Trichomonas Vaginalis and Trichomoniasis*, by Ray E. Trussell, M. D.

Williams and Wilkins Company, Baltimore: *The Scientific Paper*, by Sam F. Trelease; *Foundations of Neuro-psychiatry* (4th edition), by Stanley Cobb, A. B., M. D.



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## POLIOMYELITIS\*

BRANCH J. AYMOND, M. D.†

NEW ORLEANS

Lay groups are of the opinion that little is known about poliomyelitis. Physicians realize that a great deal is known. We have much knowledge of this disease, but like typhoid, malaria, and tuberculosis, people continue to become ill and die of these maladies throughout the world.

Historically, the first epidemic of poliomyelitis reported in the world occurred in Louisiana. Dr. George Colmer, in the year 1841, recorded his findings, after examining ten children who suddenly became ill with a fever and paralysis. Since these cases occurred during the teething period, he termed the sickness "teething paralysis." These cases occurred in Feliciana Parish, in and around St. Francisville.

The virus organism in poliomyelitis presents the same clinical manifestations in susceptible animals as in humans. The virus is highly resistant to all known chemicals. The poliomyelitis virus has been known to resist a sub-temperature of minus 70° F. Apparently the only safe poliomyelitis virus destroyer is flame heat or pressure steam sterilization. This, perhaps, is the reason why the virus is carried about, deposited, then picked up by susceptible hosts and produces poliomyelitis.

### POSSIBLE MEANS OF TRANSMISSION

*Insects:* The common housefly, in its larva stage, will grow in human excreta. Flies

caught from open back privies, where bowel content from acute and residual poliomyelitis has been deposited, have been examined and found to be carrying poliomyelitis virus. Flies are attracted to sour odors such as sewage leakage, stagnant water and garbage. In this way there is a possibility of contamination by flies of food and liquids taken into the human body.

The culex mosquito selects drainage ditches and raw sewage deposits for its larva to grow and develop into the adult mosquito. This method of transmission should always be considered—especially since a large number of acute cases seen in the Poliomyelitis Center exhibit evidence of recent mosquito bites.

*Swimming Pools:* Accepting the idea that swimming is a great muscle developer, parents are prone to encourage their children, who have had poliomyelitis, to indulge as frequently as possible in underwater exercises. Fecal examination of post poliomyelitis cases have shown that a percentage of these patients will yet be harboring the virus and for this reason swimming pools are usually closed during poliomyelitis epidemics.

*Vegetables:* Some truck farmers wash vegetables in contaminated ditches and streams in order to freshen them up. The custom of eating raw vegetables appears to be a known factor in contracting poliomyelitis.

*Milk:* Dairy cattle, in many instances, obtain their water supply from creeks, "mud holes" and collecting ground basins. The water shed may extend over a vast

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Presented at the January 27, 1947, Scientific Meeting, Orleans Parish Medical Society.

area which is contaminated by the poliomyelitis virus. It is possible for cows standing in stagnant water in the summer months to contaminate their udders with the poliomyelitis virus. At milking time little consideration is given to cleaning the udders, therefore, there is a possibility of the virus entering the human body from the milk supply. Whether or not pasteurization has adequate heat to destroy the virus is a problem for further investigation. Milk-borne transmission, perhaps, is a factor in contaminating very young babies who are totally dependent on milk for their food supply.

*Playing in Contaminated Ditches:* A "cloud burst" occurred in one of Louisiana's communities which filled a drainage ditch along one of the streets in town. The drainage flowed from open back privies used by two residual poliomyelitis patients. Six small children began playing in the accumulated water (from seven to ten day period) and the entire group of six developed poliomyelitis. They had come in contact with other children but no other cases of poliomyelitis developed during the entire year other than the children who had played in the ditch. Further, five of the six children examined had evidence of skin lacerations or abrasions, with inguinal adenitis at the time the symptoms of poliomyelitis developed.

*Closing of Schools:* Poliomyelitis usually begins about seven to ten days after school closes in summer and usually decreases by October. However, it is often necessary to close the schools for the protection of the children. Summer camps and vacation spots are a source of contamination by the poliomyelitis virus unless sanitary measures are adequately maintained.

#### SIGNS AND SYMPTOMS

To establish a diagnosis of poliomyelitis is no simple matter. The records of the Poliomyelitis Center in New Orleans reveal that 18 to 20 per cent of all cases admitted do not have poliomyelitis. This year, however, only 5 per cent admitted were found not to have poliomyelitis.

At the onset the patient usually presents a picture of a fever from 99 to 101° F. which does not respond to the ordinary antipyretics. Headaches, frontal and parietal types, usually bilateral; slight nausea, occasional vomiting with cramp-like abdominal pain; an upper respiratory manifestation, are all symptomatic.

The mother of a child sometimes recognizes these symptoms and suspects poliomyelitis. Constipation seems to be common in all poliomyelitis cases, and after two to five days, the patient will show signs of neck stiffness, back pain, and muscular disturbances.

The spinal fluid cell findings occur early and increase until the paralytic phase appears, then the lymphatic cells will begin to decrease. Usually twenty days after onset the spinal fluid findings approach normal.

#### INCREASE IN ADULT CASES

There has been a gradual increase in recent years of cases of poliomyelitis in the adult group. During the year 1946, 10 per cent of all poliomyelitis cases hospitalized at the Poliomyelitis Center at New Orleans were adults.

The fear of poliomyelitis is a natural fear. Lay groups have capitalized on this fear instead of pointing out that after all a very small per cent of an entire population are stricken.

We physicians have a mission to do in alleviating this psychological phobia in the citizen group.

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### MENINGITIS RECENT ADVANCES IN THERAPY

C. J. TRIPOLI, M. D.†

AND

W. G. UNGLAUB, M. D.  
NEW ORLEANS

The fact that the average mortality rate in cases of cerebrospinal fever (meningococcal meningitis) has declined in the

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\*Read before the scientific meeting of the Orleans Parish Medical Society, January 27, 1947.

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last 12 years from about 70 to approximately 15 per cent is in itself a distinct advance in recent therapeutics. The adventitious use of the sulfa drugs and penicillin is the basis for the remarkable improvement in the therapy of this particular type of meningitis, and in bacterial meningitis in general. In addition streptomycin has been of proved value in cases of acid fast, as well as gram-negative bacillary meningitis.

In order to evaluate the therapeutic results in cases of cerebrospinal fever and other forms of bacterial meningitis, the records of all patients with all types of meningitis treated at the Charity Hospital of Louisiana in the year 1945 have been reviewed for the present study.

In 1936 one of us<sup>1</sup> presented a comparative review of the various therapeutic procedures used in all cases of all types of bacterial meningitis treated at the Charity Hospital of Louisiana during the entire ten year period 1925-1935. This was before the introduction of the sulfa drugs or penicillin. Antimeningococcic antitoxin had been made available for use at this time and was therapeutically effective in reducing the mortality in cases of cerebrospinal fever to about two-thirds of what it had been previously, following the use of antimeningococcic serum alone.

Rollings and Musser<sup>2</sup> have presented an excellent comparative study of the incidence and treatment of the various types of meningitis in the year 1933, before the sulfa drugs were introduced, and in 1943, when the sulfa drugs, but not penicillin, were available. They reported that the mortality rate of all cases of bacterial meningitis in 1933 was 79.3 per cent; and in 1943 it had been reduced to 49.7 per cent. These figures compare closely with those reported by Waddell<sup>3</sup> who, in a similar study of mortality in cases of purulent meningitis, reported a mortality rate for all cases in a ten year period prior to the advent of chemotherapy

as 85.2 per cent, compared to 52.2 per cent for cases treated from 1937 to 1943, after sulfonamides had come into use.

The material for the present study consists of a total of 173 cases of meningitis, consisting of patients in whom the spinal fluid showed a significant increase in cells and globulin and whose clinical course was compatible with the diagnosis of acute meningitis. Of this total there were only 108 cases in which the infecting organism was identified satisfactorily in the spinal fluid by adequate smears, or by culture of the spinal fluid, or both.

Six cases were diagnosed tuberculous meningitis on the basis of the clinical findings of meningitis and characteristic findings in the spinal fluid coincidental with the existence of active tuberculosis elsewhere in the body. Four of these cases were confirmed by autopsy. Acid-fast organisms were demonstrated in the spinal fluid in only one case.

Acute lymphocytic choriomeningitis was the clinical diagnosis in four cases. Diagnosis was based on the characteristic spinal fluid cytology and the clinical course. No attempt at virus identification studies were made in these cases.

In 19 cases, organisms of various types were recorded as having been seen, but neither the morphological, tinctorial, nor cultural characteristics permitted accurate identification.

No organisms of any type could be demonstrated either in smear or culture of the spinal fluid at any time in 37 cases.

Other cases of "meningismus" and "clinical meningitis" wherein no spinal fluid studies were made are not included in this study. Also excluded are a few cases of "clinical meningitis" which died or deserted in the first twenty-four hours before spinal fluid studies were made or before any treatment was instituted.

Table 1 presents the data regarding the mortality rate in the various types of meningitis during the year 1945.

TABLE 1  
MENINGITIS  
1945

CHARITY HOSPITAL OF LOUISIANA

Type	Total Cases	Died	Mortality Per cent
Meningococcal	40	6	15.00
Pneumococcal	22	12	54.54
Streptococcal	5	1	20.00
Staphylococcal	4	3	75.00
Total coccal	71	22	32.39
Influenzal	35	20	57.14
Tuberculous	6	6	100.00
Choriomeningitis	4	0	0.00
Torula	1	1	100.00
Organism not definitely identified	19	3	15.79
No organism found	37	17	45.94
Total cases	173	69	39.88

There was a total of 40 patients with cerebrospinal fever or meningococcal meningitis. Six of these patients died resulting in a mortality rate of 15 per cent. Twenty-one of these patients received only a sulfa drug, usually sulfadiazine, orally alone or with initial intravenous sodium sulfadiazine. All of these 21 persons recovered. The result in these cases is the same as that reported for 1940-41<sup>4, 5</sup> under a similar form of therapy. The remaining 19 patients received the sulfa drug orally and in a few instances intravenously in addition to penicillin intramuscularly and intrathecally. The intrathecal use of penicillin was usually limited to an initial dose except in a few instances wherein it was used once or twice daily for a few days. Six of the patients so treated died. Although, at first glance one may conclude that intraspinal penicillin therapy is harmful in cases of cerebrospinal fever, one must consider the fact that in most instances the desperately ill patients received the additional therapy, whereas those who manifested clinical improvement on sulfa alone were not even considered as candidates for additional intrathecal therapy. However, there is no evidence to prove that intraspinal therapy of any type is of any value in the treatment of cerebrospinal fever. Of additional importance is the fact that there is evidence which indicates that the sulfa drugs intraspinally are not only of no value, but in addition, produce unfavorable reactions which are apparently harmful. The administration of penicillin

intrathecally in cases of cerebrospinal fever has been of no proved value and reports of harmful reactions have been presented.<sup>6</sup> In the study of this series of 40 cases of cerebrospinal fever treated over a period of one year, there is no evidence to support the opinion that penicillin intrathecally is of any value in this disease. However, neither do we find in this series any evidence of any immediate unfavorable reactions. It is a fact that penicillin, parenterally administered, does not usually appear in the spinal fluid in effective concentrations,<sup>7</sup> and it is evident that intraspinal administration is definitely indicated and beneficial in cases caused by coccal organisms other than meningococci. But we repeat that this does not hold true for cerebrospinal fever. In spite of these facts it is difficult to resist the obvious temptation to use penicillin intrathecally in cases of cerebrospinal fever.

There were 22 patients with pneumococcal meningitis, 12 of whom died, resulting in a mortality rate of 54.5 per cent. Two of the patients who died received only sulfa orally and parenterally, and three received intrathecal penicillin in addition to sulfa orally and parenterally, one of whom received intracisternal penicillin. Another two of the 12 patients received sulfa orally and parenterally and additional penicillin intramuscularly as well as intrathecally. The remaining five of the 12 persons who died received antipneumococcal serum intravenously and intramuscularly in addition. The ten who survived received sulfa orally and parenterally, penicillin intramuscularly and intrathecally. Two of these ten patients received additional antipneumococcal serum. This mortality rate of 54.5 per cent in 1945, when both sulfa and penicillin were used, is a distinct improvement over the mortality rate of 72 per cent in the 1943 series, wherein sulfa alone was administered.<sup>2, 3, 8</sup> The use of penicillin in addition to sulfa is the apparent reason for the improved results. Appelbaum and Nelson<sup>9</sup> reported a mortality rate of 61 per cent in a series of 67 cases using a similar routine of therapy.



There were five patients with streptococcal meningitis, one of whom died, resulting in a mortality rate of 20 per cent. All of these persons received sulfa orally and parenterally. Four of the five received additional penicillin intrathecally. Three of the five patients received additional intramuscular penicillin. One of the latter three patients died. Similar reports have been presented.<sup>8</sup>

There were four cases of staphylococcal meningitis and three deaths, the mortality rate being 75 per cent. All four patients received sulfa orally and parenterally and intramuscular penicillin. Only two received additional intrathecal penicillin; one of the latter recovered. In all of these cases positive blood cultures were obtained. It is to be noted that the average mortality rate is much higher in this type of case associated with septicemia than in those cases of meningitis resulting from direct extension of infection to meninges from the bony structures of the mastoids or paranasal sinuses, without septicemia.<sup>8</sup>

There were 35 cases of influenzal meningitis. Thirty-three cases were found to be Type B and and two cases were unfortunately not typed or recorded. Twenty of these 35 patients died, resulting in an average mortality rate of 57.14 per cent. Twenty-two of the total patients received sulfa orally and parenterally plus anti-influenzal serum type B intravenously or intramuscularly. Eight of these 22 patients received additional serum intrathecally. There were 15 deaths and seven recoveries from this group of 22 cases. The remaining 13 patients received sulfa orally and parenterally plus penicillin either intramuscularly or intrathecally or both. Of the 13 patients five died and eight recovered. Seven of this latter 13 received additional anti-influenzal serum Type B. Of the seven who received this serum, three died and four recovered. Of interest is the fact that of the 35 patients only two were over three years of age. One of these was 27 years of age and the other 63 years; both recovered and are included in the appropriate group. Only two of the 35 patients had

positive blood cultures, one died and one recovered. No streptomycin was available for use in these cases.

There were six cases of tuberculous meningitis. Two of these patients received only supportive therapy. Two received sulfa alone. One received sulfa and intramuscular penicillin. One received sulfa intramuscularly and intrathecal penicillin. All patients died. No streptomycin was available for use in this group.

There were four patients with acute lymphocytic choriomeningitis. One received no treatment. One received sulfa orally and parenterally. One received sulfa orally and parenterally and penicillin intramuscularly; and one received sulfa orally and parenterally and penicillin intrathecally. All patients recovered. The results in these series are identical with a previous series reported by one of us<sup>10</sup> in which treatment consisted of only supportive therapy after initial diagnostic spinal puncture was done. Chemotherapy, as well as antibiotic therapy, is apparently superfluous in the treatment of this disease.

Only one case of torula meningitis was treated during this time. Sulfa orally and parenterally and penicillin intramuscularly and intrathecally were employed. This patient showed no response and died.

Of the 19 cases of meningitis produced by demonstrable organisms which were not definitely identified there were three deaths. Eleven of the total 19 patients received sulfa orally and parenterally alone, and one received additional antimeningococcic antitoxin. No deaths occurred in this group of eleven patients. The remaining eight received sulfa orally and parenterally and penicillin intrathecally. Five received additional intramuscular penicillin. Of this group of eight patients there were three deaths.

No organisms were demonstrable at any time in the abnormal spinal fluid of 37 patients with clinical meningitis, of whom 17 died. Two of the total number of patients received no treatment and died. Twenty-four of the remaining 35 patients received sulfa orally and parenterally, one of whom

received additional anti-influenzal serum intrathecally. There were ten deaths in these 24 persons. Of the remaining eleven patients, five received sulfa orally and parenterally and intramuscular penicillin, with three deaths; two received sulfa orally and parenterally with penicillin intrathecally with no deaths; four received sulfa orally and parenterally and penicillin intramuscularly and intrathecally with two deaths.

The use of heparin intrathecally in addition to routine sulfa and penicillin has been recommended <sup>11, 12</sup> in the treatment of those cases of purulent meningitis in which fibrin formation and coagulation were the probable causes of a possible partial or complete block in the cerebrospinal fluid circulation. There were four cases of influenzal meningitis in which a single dose of heparin was given intrathecally. The dosage in two of the patients was 2.0 mg. each; and in the other two patients 10 mg. and 5 mg. respectively. Two patients recovered and two died. Three persons with meningococcal meningitis received heparin intrathecally in doses of 2 mg. -5 mg. -10 mg. respectively, in addition to the sulfa and penicillin routinely; two patients recovered and one died. One patient with pneumococcal meningitis received a 2 mg. dose of heparin intrathecally in addition to the routine of sulfa and penicillin. This man recovered. One patient with a coccal (type not identified) meningitis received a 5 mg. dose of heparin intrathecally in addition to the routine sulfa and penicillin therapy. This person died. Obviously the use of heparin and other anticoagulants intrathecally in these patients has not been of any remarkable therapeutic benefit. However, the exact dosage or mode of administration with and without dicoumarin has not been completely worked out. In addition it will be necessary to control carefully the effective dosage in order to prevent possible untoward results from overdosage.

The advent of streptomycin and its effective use in tuberculous meningitis has aroused considerable interest. Because streptomycin does not appear in the spinal

fluid in effective therapeutic concentration it is necessary to administer it intrathecally as well as parenterally.<sup>13</sup> Henshaw et al.<sup>14</sup> have reported a series of seven cases of tuberculous meningitis, proved by demonstration of the acid-fast organisms in the spinal fluid, treated with apparently adequate doses of streptomycin. Four of the seven patients have survived the disease over a period of three to six months after treatment. The treatment consists of 100-200 mg. doses of streptomycin intrathecally daily over a period of two or four weeks and 1.2 to 3.6 gm. daily intramuscularly over a period of three to six months. All of these patients had evidence of generalized hematogenous miliary tuberculosis in addition to meningitic involvement. At the time of the report all four patients continued to have clinical abnormalities indicating persistence of residual infection despite treatment but the organisms could no longer be isolated from the spinal fluid by culture or animal inoculation.

Streptomycin in influenzal meningitis is apparently the antibiotic of choice. It has been given in doses varying from 15,000 to 125,000 units every three hours intramuscularly, simultaneously with intrathecal administration of amounts varying from 10,000 to 25,000 units every 24 hours <sup>15, 16</sup> resulting in a 25-50 per cent reduction in the average mortality rate. Equally remarkable beneficial results have been reported following the use of parenteral anti-influenzal serum type B in addition to sulfadiazine in cases of this type of influenzal meningitis.<sup>17</sup> Under proper control it would appear that a combination of these two effective therapeutic programs would be the treatment of choice.

In reviewing the histories of many of these cases it frequently occurred that the patient received apparently inadequate doses of either the sulfa drugs or antibiotics before admission to the hospital. Just what, if any, effect this had on the course of the disease cannot be determined in any case or cases of this series. However, it is apparent that benefit from both sulfa drugs and antibiotics only results when effective



doses are used; and if they are to be given the dosage should always be adequate.

#### SUMMARY AND CONCLUSIONS

A review of the results of therapy used in 173 patients with meningitis of the various types treated in Charity Hospital of the State of Louisiana during the year 1945 is presented.

The mortality rate in 40 patients with cerebrospinal fever (meningococcal meningitis) treated during this period averaged 15 per cent. This reduction, as compared to an average mortality rate of 70 per cent during the year 1933 has been achieved by the adequate use of the sulfa drugs, principally sulfadiazine, and penicillin. There is no indication for the use of either of these therapeutic agents intrathecally in this type of meningitis.

The mortality rate in 22 patients with pneumococcal meningitis treated during this period averaged 54.54 per cent. This reduction, as compared to a mortality rate above 90 per cent during the year 1933, is a direct result of the use of adequate doses of the sulfa drugs orally and parenterally and penicillin parenterally and intrathecally. It is apparent that the additional intrathecal use of penicillin is necessary in the treatment of this type of meningitis.

The mortality rate in staphylococcal and streptococcal meningitis has been reduced at least 50 per cent by the similar program of treatment as used in the pneumococcal type of meningitis. It is apparent that detailed studies regarding the individual bacterial penicillin sensitivity of the individual organisms isolated in each case will be of great value in estimating the penicillin dosage to be used in any one patient. No efforts have been made in this series to determine any definite effect in the penicillin sensitivity of the staphylococcal or streptococcal organisms in any of the individual patients. Therefore, we are unable to tell in the persons who died whether or not adequate doses of penicillin were given.

The mortality rate in 35 patients with influenzal meningitis treated during this period averaged 57.14 per cent as compared

to a mortality rate of 90 per cent during the year 1933. Of the various routines of treatment it appears that the use of streptomycin and anti-influenzal serum in influenzal type B cases is the treatment of choice.

The mortality rate in six patients with tuberculous meningitis treated during this period has remained 100 per cent. No streptomycin was used in any of these patients. It appears that this therapeutic agent at present is the only treatment having considerable therapeutic merit. Although the course of the disease has been favorably affected, it is necessary to continue use of the drug over a period of months. Neurologic residua are the rule and only in a few proved cases so far has the disease apparently been completely arrested and the patient's spinal fluid and clinical condition apparently returned to normal. The promise which this type of therapy offers in this most serious disease is anticipated with great interest.

The mortality rate in four cases of acute lymphocytic choriomeningitis treated during this period has remained zero. Since this type of meningitis is self-limited and almost invariably ends in recovery, the use of the sulfa drugs and penicillin was obviously superfluous but not harmful.

In those cases of purulent meningitis in which no organisms were demonstrable in the spinal fluid or wherein organisms were apparently seen but not positively identified, the average mortality rate has been reduced to between 15 and 45 per cent. It is not possible to determine whether these cases were primary meningitis or had any associated septicemia. The treatment of choice appears to be the same as that used for the pneumococcal, streptococcal and staphylococcal types of meningitis.

It appears that those cases of bacterial meningitis other than meningococcal wherein the organisms subsequently invaded the subarachnoid space from the paranasal sinuses or mastoids have a more favorable prognosis under this form of therapy

than those resulting from generalized septicemia.

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### PERITONEOSCOPY

#### AN ANALYSIS OF ITS USE IN SIXTY-NINE CASES

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AND

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SHREVEPORT

Peritoneoscopy is not a new procedure, having been first demonstrated by Kelling about 46 years ago.<sup>10</sup> However, it is surprising to see the lack of appreciation of

the value of this procedure as a method of endoscopic diagnosis and we are in accord with Beling<sup>6</sup> who feels that if its advantages and indications were better understood it would receive proper recognition. Ruddock<sup>2</sup> deserves the credit for creating a firm foundation and stimulating the clinical use of the procedure in this country. He devised a special instrument and defines the procedure as visualizing the peritoneal cavity and its contents by means of an optical instrument.

In April, 1944 one of us (W. H. B.) instituted the use of this procedure in Shreveport Charity Hospital as an accessory means in the diagnosis of obscure abdominal disease and up until March, 1947 it had been used in 69 cases with gratifying results. From our experience thus gained we feel that it deserves the credit and recognition accorded to other methods of endoscopy.

The indications for the use of the procedure can best be given in a list form, and comments concerning each given later. The indications are as follows:

1. Diseases of the peritoneum.
2. Gastric malignancy; that is, ruling out metastatic disease before operation.
3. Liver disease.
4. Unexplained ascites.
5. Pelvic pathology; that is, suspected ectopic pregnancy and ovarian tumors.
6. Undiagnosed abdominal masses.
7. Gunshot and stab wounds of the abdomen with doubtful penetration.
8. Non-penetrating trauma when internal injury is suspected, particularly of the liver or spleen.
9. Differentiation between bleeding peptic ulcer and esophageal varix.

In two diseases of the peritoneum peritoneoscopy is especially valuable in diagnosis and it is helpful in the treatment of one. Carcinomatosis secondary to any source is readily diagnosed by this method. Ruddock<sup>2</sup> has reported a peritoneoscopic accuracy of 87.03 per cent in the diagnosis of 54 proven cases of peritoneal metastases. Tuberculous peritonitis prior to peritoneoscopy was usually diagnosed by laparotomy

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and a number of patients seemed to improve after this procedure, at which time atmospheric air was admitted into the peritoneal cavity. Beling<sup>6</sup> feels that it is no longer necessary or advisable to subject these patients with tuberculous peritonitis to the hazards of laparotomy. With the peritoneoscope a definite diagnosis can be made and a pneumoperitoneum produced as a method of treatment. Ruddock<sup>2</sup> has also reported a peritoneoscopic accuracy of 66.67 per cent in the diagnosis of 18 proved cases of tuberculous peritonitis. We have had the good fortune of observing two of four cases of tuberculous peritonitis, diagnosed by this method, over one year after their diagnosis and therapeutic pneumoperitoneum. One had a mild exacerbation of the disease that responded to rest in bed and the other was well with no evidence of disease and had gained 30 pounds in weight.

Benedict<sup>8</sup> reports that during a five year period (1937-1941), 263 patients with cancer of the stomach were explored surgically without peritoneoscopy and 30, or 15 per cent, of the patients were inoperable because of liver metastases. He also reported the performance of peritoneoscopy in 95 cases of carcinoma of the stomach, the results of which showed 20 cases with metastatic disease, thus avoiding a useless laparotomy in 21 per cent of the 95 cases. However, Beling<sup>6</sup> emphasizes the differentiation of carcinoma of the stomach into obstructive and non-obstructive types for peritoneoscopic purposes. It is obvious that in the obstructive type peritoneoscopy is contraindicated because operation is inevitable for restoration of the continuity of the gastrointestinal tract. Ruddock<sup>2</sup> has described transillumination of the stomach at the time of peritoneoscopy to determine the extent of involvement of the organ. Priestley<sup>5</sup> states that the determination of operability of gastric carcinoma by means of peritoneoscopy, based only on the local extent of the primary disease, is definitely unwise but feels that it may be a sound procedure if based on the presence of metastatic lesions. Oaks<sup>10</sup> also emphasizes that peritoneoscopy for this purpose is a super-

fluous procedure in the case of gastric carcinoma with obstruction because surgical intervention is necessary.

Perhaps the most efficacious use of peritoneoscopy is in the diagnosis of diseases of the liver. In a series of 435 peritoneoscopies at the Massachusetts General Hospital the question of liver disease arose in 331, or 70 per cent.<sup>8</sup> There were proved by peritoneoscopy, in this series, 260 cases of liver disease of which 83 were non-malignant and 177 were malignant disease. There were five primary carcinomas in the 177 malignant cases. In 71 cases the liver was essentially normal. Wershub<sup>9</sup> reports similar results in a series of 100 peritoneoscopies, 54 of which were related to the liver. Thirty-five cases of cirrhosis were encountered in this group and 14 cases of secondary carcinoma were diagnosed by this method. Five miscellaneous diseases of the liver were encountered. Also in Wershub's<sup>9</sup> series there were four cases of hydrops of the gallbladder diagnosed by this method. Benedict<sup>3</sup> has reported the diagnosis of a polycystic liver by this method of endoscopy. Ruddock<sup>2</sup> has reported a peritoneoscopic accuracy of 87.4 per cent in the diagnosis of 79 proven cases of malignancy of the liver. Benedict<sup>3</sup> has emphasized the proper preparation of patients with liver disease before doing peritoneoscopy by administering vitamin K and avoiding morphine and the barbiturates as sedatives, substituting chloral hydrate for this purpose. Ruddock<sup>2</sup> feels that all patients with a diagnosis of suspected cirrhosis of the liver should be examined with the peritoneoscope for corroboration.

With regard to the use of the method in unexplained ascites, the accuracy is related to the disease processes causing the condition and they have been referred to in the foregoing remarks. Perhaps the most common causes for ascites are: (1) cirrhosis; (2) carcinomatosis; and (3) tuberculous peritonitis. Beling<sup>6</sup> feels that abdominal paracentesis is a useless procedure if peritoneoscopy is contemplated because that is accomplished at the same time as the examination.

Hope<sup>1</sup> has reported favorably on the use of the procedure in the diagnosis of ectopic gestation and emphasizes that at times this can be one of the most difficult diagnoses in the field of gynecology. Ruddock<sup>2</sup> reports a peritoneoscopic accuracy of 100 per cent in 13 proved cases of ectopic pregnancy. Usually the ectopic gestation can be seen but in any case with a suitable history the finding of a hemoperitoneum is sufficient evidence and operation is performed. It should be emphasized that peritoneoscopy is not recommended as the diagnostic method in the ordinary case but is reserved for the cases in which the diagnosis is difficult. Other pelvic pathology such as ovarian tumors and cysts are frequently diagnosed by this method. Hamilton<sup>7</sup> has used the procedure in the diagnosis of salpingitis, appendiceal peritonitis, appendicitis, cholecystitis, and has designed a manipulating rod and an insulated endothermy electrode for facilitating the examination of the abdominal organs and dividing adhesions respectively. He has also reported the puncture of an ovarian cyst in a case of severe menorrhagia with good results for six months, the endometrium changing from hyperplasia to hypoplasia. Benedict<sup>3</sup> has reported the aspiration of a large benign ovarian cyst in an 89 year old female with alleviation of symptoms. Five hundred and twenty cubic centimeters of fluid were obtained. This procedure was performed because it was thought that the patient's general condition would not allow surgery.

Undiagnosed abdominal masses are usually satisfactorily elucidated by peritoneoscopy except those that are retroperitoneal and occasionally they can be diagnosed if they have metastasized to the liver or structures that can be biopsied.

Beling<sup>6</sup> feels that gunshot or stab wounds of the abdomen contraindicate peritoneoscopy but Hamilton<sup>4</sup> has reported the successful management of five cases with this method. Hamilton,<sup>4</sup> however, emphasizes that this method is not applicable if the patient is in desperate condition, if perforation is obvious, if there is a perforation of

the diaphragm (production of a pneumothorax when air is injected into the abdomen), and if the wound is posteriorly situated. He cites the figures of the results in 114 operations at Louisville City Hospital, over a three year period, for stab and gunshot wounds of the abdomen in which 24, or 21 per cent, were found not to penetrate the peritoneum. An analysis of these 24 negative exploratory laparotomies revealed that in all but one the perforation, if present, could have been visualized by examination with the peritoneoscope. The presence of a hemoperitoneum or the visualization of a peritoneal laceration is definite indication for exploration. For the details of the examination as described by Hamilton<sup>4</sup> the reader is referred to his article.

Hamilton<sup>4</sup> feels that the findings at peritoneoscopy in cases of nonpenetrating abdominal trauma should be interpreted with caution, however, the discovery of a laceration of the bowel or stomach constitutes a clear-cut indication for operation but the failure to find the injury to the hollow viscera by no means rules it out. He reports the successful use of peritoneoscopy in one case with two lacerations of the liver that were repaired at operation.

Hamilton<sup>7</sup> also has reported on the successful use of the peritoneoscope in differentiating between bleeding peptic ulcer and ruptured esophageal varix. The finding of a typical hobnail cirrhotic liver is indicative of bleeding esophageal varices. He feels that this procedure is less likely to restart or to aggravate bleeding and is more certain in diagnosis than the alternative barium swallow proposed by Schatzki.

The contraindications to peritoneoscopy will be given in a list form as follows:

1. The acute abdomen.
2. Hemorrhagic states.
3. Advanced cardiac and pulmonary disease because of embarrassment of circulation or respiration, due to the pneumoperitoneum.
4. Extensive bowel adhesions.

The only fatality in our series of 69 cases was related to the contraindication listed



under number 3 and will be considered later.

The complications of the procedure are varied and the following have been reported:

1. Perforation of the bowel.
2. Subcutaneous emphysema.
3. Bleeding from the site of the biopsy.
4. Bile fistula from liver biopsy in obstructive jaundice.
5. Pneumothorax in a patient with a penetrated diaphragm from a gunshot wound of the abdomen.
6. Hernia through the puncture wound.
7. Hematoma at the site of the puncture wound.

Ruddock<sup>2</sup> has reported eight cases of puncture of the bowel in 500 examinations and in each instance the bowel was firmly plastered against the parietal peritoneum. Hematoma at the site of the wound occurred in two of his cases but herniation through the scar of the puncture wound did not occur in his series of cases.

Benedict<sup>8</sup> reported three deaths, in a series of 435 peritoneoscopies, that were considered attributable to the procedure. One death was due to heart failure in a patient with multiple lung abscesses, coronary disease and possible echinococcal cyst of the liver; the second a death due in part to hemorrhage eight days after liver biopsy in a case with extensive metastatic carcinoma; and the third three weeks after perforation of the large bowel in a severely ill patient proved by peritoneoscopy to have advanced tuberculous peritonitis.

For descriptions of the procedure and the instrument the reader is referred to the articles listed under references. However, it will suffice to say that the procedure is carried out in the operating room under local anesthesia after preparation of the abdomen as for a laparotomy and the administration of the usual preoperative sedation. The site of insertion of the instrument is about one and a half inches below and to the right of the umbilicus.

#### RESULTS IN SIXTY-NINE CASES

In this series of 69 cases there were two ectopic pregnancies encountered, one of

which showed a hemoperitoneum at peritoneoscopy and an immediate laparotomy showed a ruptured tubal pregnancy for which a salpingectomy was done. The other case had inconclusive findings at peritoneoscopy but was diagnosed by cul-de-sac aspiration with blood being obtained. An exploratory laparotomy and salpingectomy was performed. One case with a generalized carcinomatosis was shown to have metastatic carcinoma of the liver and a subsequent laparotomy revealed a pelvic mass considered to be the source of the metastases. One case showed a pelvic mass at peritoneoscopy but no biopsy could be taken and a subsequent laparotomy revealed a dermoid of the ovary with malignant changes in the form of squamous carcinoma. One peritoneoscopy revealed a pseudomucinous cystadenoma of the ovary; no biopsy was taken, and later a laparotomy was done with the excision of the tumor and x-ray treatment later. A case of squamous carcinoma of the cervix with a questionable mass was examined and a mass in the broad ligament was observed but no biopsy taken because of adhesions. A five year old white female was examined and an enlarged right ovary was seen, the patient discharged to return in six weeks for laparotomy but there was no record of the return visit. One case of adenocarcinoma of the uterus with extension to the vaginal wall was examined and an ovarian tumor was seen; no biopsy was taken but the abdominal fluid was positive for tumor cells. One cystadenocarcinoma of the ovary was diagnosed by peritoneoscopy; no biopsy taken, being proved by a subsequent laparotomy.

There were two cases of a retroperitoneal mass being diagnosed by peritoneoscopy. One later at laparotomy proved to be adenocarcinoma grade 2 of undetermined origin, and the other at autopsy as being due to metastatic carcinoma from the prostate. One case of carcinoma of the pancreas was examined unsuccessfully: a later laparotomy proving the diagnosis. One patient with pulmonary tuberculosis was examined and a cystic paravertebral mass was found;

no biopsy was taken and the patient subsequently was discharged without a diagnosis being made.

One case with a mass in the left upper quadrant was examined at which time it was seen to be retroperitoneal in the kidney region and subsequently a nephrectomy of the left kidney was performed for hydronephrosis. One examination disclosed splenic adhesions and the patient was discharged with the diagnosis of perisplenitis. One examination disclosed omental adhesions and the patient was later subjected to a vaginal myomectomy. One examination in a case of metastatic umbilical carcinoma showed no definite findings except a scarred area in the pylorus of the stomach. One adenocarcinoma of the rectum was examined before considering radical resection and metastatic disease of the liver was found, thus eliminating a useless radical procedure; later colostomy was done for obstructive symptoms.

There were 10 cases in which peritoneoscopy revealed no definite findings and no biopsies were taken. These cases will be tabulated in list form:

1. Unexplained chronic abdominal pain with a negative physical examination. A single uterine adhesive band was found, thought not to be clinically significant.

2. Hypertensive cardiac disease with recurrent ascites despite adequate digitalization. Clinically an ovarian tumor was suspected but peritoneoscopy revealed no pathology.

3. Suspected ascites but examination revealed no findings.

4. Carcinoma of the colon, suspected, but no findings by peritoneoscopy. Discharged undiagnosed.

5. Normal pregnancy, but a hydatidiform mole with malignant degeneration was suspected due to an abnormal menstrual history. Examination showed a normal uterine pregnancy.

6. One case of questionable intra-abdominal disease but examination showed no findings.

7. Bronchogenic carcinoma with widespread metastases proved at autopsy;

question of metastatic abdominal disease, site of origin undetermined ante mortem, with positive aspiration from mass in right flank showing malignancy. Peritoneoscopy showed no intra-abdominal disease.

8. Hepatomegaly with an undiagnosed parotid gland tumor. Peritoneoscopy showed no intra-abdominal disease.

9. Undiagnosed febrile illness with hepatomegaly. Peritoneoscopy revealed no findings but autopsy showed miliary tuberculosis and a cavernous hemangioma of the liver.

10. Threatened early abortion confused with an ectopic gestation. Friedman test positive. Peritoneoscopy revealed no findings.

There were 34 liver biopsies taken in this series of 69 cases. Ten of these were inconclusive, one of which was later diagnosed by aspiration biopsy as an angioma of the liver. Two biopsies were reported as normal liver and there were three records which had no report of the biopsy on the chart. Seven biopsies were positive for cirrhosis of the liver. One biopsy was positive for cirrhosis of the liver and serositis as seen in Pick's disease. One was positive for carcinoma in a cirrhotic liver. Five showed metastatic carcinoma. One each showed hepatitis, gumma, primary carcinoma, and sarcoidosis. One biopsy was reported as metastatic angiosarcoma but later at the time of exploratory laparotomy a primary lesion of the stomach was removed, which showed a vascular leiomyosarcoma that was interpreted as being the tumor from which the metastases came. Excluding the three biopsies of which no reports were found, a positive histologic diagnosis was made in 61.3 per cent of the cases.

There were nine biopsies of the peritoneum, of these one was inconclusive. There was no report of one. Four showed tuberculous peritonitis. Two showed metastatic carcinoma and one showed metastatic leiomyosarcoma. Excluding the one biopsy of which there was no report on the chart, a positive diagnosis was obtained in 87.5 per cent of peritoneal biopsies.



One biopsy of a pedunculated nodule in the pelvis was reported as consistent with leiomyosarcoma. One omental biopsy was inconclusive and one biopsy of a pelvic sacral mass was reported as metastatic carcinoma. Two spleen biopsies were reported as showing fibrosis.

In the total series of biopsies, excluding those of which there were no reports, a positive diagnosis was obtained in 63.6 per cent of the cases.

In reviewing the clinical data in these 69 cases the indications for these examinations were as follows:

1. Unexplained ascites.
2. Undiagnosed abdominal mass.
3. Suspected cirrhosis of the liver.
4. Suspected pelvic pathology.
5. Determination of operability in gastrointestinal malignancy.

In this series of 69 cases there were four complications observed, a total of 5.8 per cent. Two of these were of minor importance, being subcutaneous emphysema which subsided spontaneously in a few days' time. One was a hematoma around the site of the abdominal wound and moderate bleeding into the peritoneal cavity from the biopsy site. This patient had metastatic carcinoma to the liver. He died several weeks later, his death not being attributed to this complication. One case in which death occurred two and one-half days after the examination due to recurrent shock is considered as a fatality in this series. This patient had tuberculosis of the lung with cavitation and far advanced cirrhosis of the liver. Consequently the mortality rate of this series is 1.4 per cent.

Only 12, or 17.4 per cent, of the 69 cases were subsequently subjected to a laparotomy for either diagnostic or therapeutic purposes. This is not considered frequent enough to detract from the procedure as a primary method of diagnosis.

#### ILLUSTRATIVE CASES

##### CASE NO. 1

A 57 year old white male was admitted to the hospital on October 12, 1946, with the complaint of pain in the right lumbar region for three weeks. He had a past history of carcinoma of the nose.

Examination revealed a one centimeter ulcer on the right side of the nose and a 5.5 by 1.5 centimeter ulcer encircling the right leg. The liver was felt 10 centimeters below the costal margin. A biopsy of the nasal lesion showed basal cell carcinoma. At peritoneoscopy, the liver was greatly enlarged with large nodules on the surface. A biopsy was taken and reported as anaplastic small cell carcinoma. He was discharged on December 10, 1946.

##### CASE NO. 2

A 44 year old white male was admitted February 9, 1945, with a pain in the abdomen for six weeks, vomiting at the onset of the illness, and progressive swelling of the abdomen. There was a history of alcoholism. Examination showed a distended abdomen with a fluid wave, no organs being palpable. At peritoneoscopy, the liver was small with coarse lobulations. A biopsy was taken from the liver and the pathologic report was cirrhosis of liver. He was discharged February 22, 1945.

##### CASE NO. 3

A 19 year old colored female was admitted December 29, 1945, with the chief complaint of an abdominal mass for one year, occasional vomiting, bleeding gums and excessive menses for two or three weeks. Examination showed a few nodes in the neck, mandibular, and inguinal regions. The liver was palpable four fingers below the rib margin and the spleen was not definitely felt. The blood count, urinalysis, and liver function tests were normal. The Kahn and Wassermann were four plus. A peritoneoscopic examination and liver biopsy on January 16, 1946, were inconclusive except for the finding of a greatly enlarged and coarsely nodular liver. A repeat peritoneoscopy on January 31, 1946, showed the same findings and a non-umbilicated area on the left side of the interlobar fissure was biopsied. The pathologic report was carcinoma consistent with hepatic origin. She was discharged on February 11, 1946.

##### CASE NO. 4

A 25 year old colored female was admitted on October 3, 1945, with the complaint of abdominal pain and swelling of the abdomen for three weeks, associated with headache. Examination showed a distended abdomen with a fluid wave and shifting dullness. An EPA of the chest was negative. At peritoneoscopy on October 11, 1945, small excrescences on the peritoneum, uterus, tubes, and left ovary were seen. The peritoneum over the uterus was biopsied, and the pathologic report was tuberculosis. She was discharged on October 16, 1945, with the diagnosis of tuberculous peritonitis.

##### CASE NO. 5

A 47 year old colored female was admitted to the hospital on February 8, 1947, with the history of a chronic illness for three years. She complained of a chronic cough with an occasional hem-

optysis, pain in the chest, 75 pounds of weight lost, and intermittent fever with an occasional chill. Within the past few months epigastric pain, nausea and vomiting had occurred and reddish brown plaque-like lesions had developed on the face and trunk. Examination showed the previously described skin lesions, a pterygium on the right eye, cervical and inguinal adenopathy, enlarged parotid gland, tubular breath sounds in the hilar regions, a liver palpable below the umbilicus and an ulcerated lesion on the posterior lip of the cervix. An EPA showed hilar adenopathy and infiltration in the right lung field. The total protein was 9.53 grams with 3.5 grams of albumin. The clinical diagnosis was Boeck's sarcoid. On February 13, peritoneoscopy was done, at which time the liver was greatly enlarged and was covered with a grayish, white fibrinous exudate. The surface was firm. The spleen was normal. Biopsy of the liver was done and the pathologic report showed Boeck's sarcoid. Subsequent skin and cervical biopsies were inconclusive for Boeck's sarcoid. She was discharged on March 7, 1947, as generalized sarcoidosis.

## CASE NO. 6

A colored female, aged 37, was admitted January 28, 1947, with the complaint of a "knot" in the epigastrium associated with a dull pain for one month. Examination showed a nodular tumor in the epigastrium that moved with respiration. A lower midline scar was present at the site of a previous operation for a hysterectomy. Pelvic examination showed a normal cervix. The Wassermann was four plus. Peritoneoscopy on February 5, 1947, showed the liver to be enlarged four fingers below the costal margin and three whitish nodules present, two in the right lobe and one in the left lobe. The mass in the left lobe was biopsied and the pathologic report was consistent with gumma. She was discharged February 17, 1947, with the diagnosis of gummata of liver.

## SUMMARY

In conclusion we have presented a brief analysis of 69 peritoneoscopies and have referred briefly to the literature. From the above data it is felt that peritoneoscopy is a valuable type of endoscopic examination when the indications for its use exist.

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## ACUTE MASTOIDITIS\*

## SECONDARY TO FRACTURE OF THE MASTOID

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NEW ORLEANS

This is a case of a simple fracture of the mastoid, which with its disturbed physiology, breaking down of normal barriers to the spread of infection, and hematoma formation made an ideal environment for the rapid spread of superimposed infectious process in the mastoid.

## REPORT OF A CASE

An 11 year old colored male was first seen on Saturday, March 29, 1947, complaining of severe pain in the left ear. He had been struck two months prior to that date by a golf club over the left mastoid. There was pain, swelling, and redness in this region lasting for approximately one week and then subsiding. There was no discharge of any sort from the ear at this time.

Three weeks before coming to the hospital the patient developed left otalgia with purulent discharge while suffering a cold in the head. He had been treated by his local physician with white tablets and a liquid medicine. The otalgia and discharge had subsided in five days.

Two days prior to admission pain again started in the left ear with swelling behind it and fever.

His review of other systems, family and social histories were non-contributory.

In his past history there was no suggestion of otological pathology prior to the present illness.

Upon arrival at the ward his temperature was 100.2° F. His pulse rate was 120, and his respiratory was 22. In general, he appeared to be a rather well-developed, though somewhat thin colored male of about his stated age of 11 years. He did not appear acutely ill. Positive physical findings were limited to the left ear and mastoid ex-

\*Read before the E. E. N. T. Staff of Charity Hospital, New Orleans, May 21, 1947.



cept for a slight pharyngeal infection and a left precervical lymphadenopathy. Examination of the heart and lungs was clinically negative, and fundoscopic examination revealed no vascular congestion or papilledema.

Hearing was somewhat decreased in the left ear. There was angulation of the auricle, with post-auricular redness, heat, and swelling. Tenderness was present over the tip and antral regions, though more exquisite over the antrum. Fluctuation was also noted over the region of the antrum. There was a sagging of the posterior-superior external auditory canal wall. The tympanic membrane was dull, thickened, red, and bulging, the bulging being more pronounced in the attic region.

Roentgenograms taken on admission consisted of Law views of the mastoids, posterior-anterior and left lateral views of the skull, and an erect posterior-anterior view of the chest. With the assistance of the two radiologists on duty that Saturday afternoon these films were examined. No fracture line was identified. Only clouding with loss of cellular detail and destruction in the left mastoid was identified. The chest plate revealed no pathology.

Hematologic examination performed on admission showed a red blood count of 3,800,000, a white blood count of 9200 with 76 per cent polymorphonuclear leukocytes, 2 per cent eosinophiles, and 22 per cent lymphocytes. Urinalysis was negative. Blood for Kline test taken on admission was later reported as negative. A blood culture taken on admission was also later reported as negative.

On the afternoon of arrival at the hospital (March 29, 1947) a preoperative diagnosis of acute mastoiditis with post-auricular subperiosteal abscess was made and the patient scheduled for a simple mastoidectomy that afternoon. The left mastoid region was shaved in the customary manner, and the patient was pre-medicated with 1/400 grain of atropine sulfate. Under vinethene and ether vapor general anesthesia, the left mastoid region was prepared with ether and merthiolate tincture and draped in the usual manner.

A myringotomy was performed at the site of preference freeing sero-sanguinous exudate. Culture was sent to the Pathology Department which was later reported "no growth."

A Beck type post-auricular mastoid incision was made down through the periosteum. A sub-periosteal abscess was entered freeing frank yellow pus. A specimen of this pus was sent also to the Pathology Department, also later reported, "no growth." A fracture was found extending through the posterior bony canal wall above and extending posteriorly and inferiorly downward across the tip of the mastoid. A dehiscence was present in the inferior part of the sieve area through which purulent exudate exuded. This defect was from 8-10 mm. in diameter. Some attempt at callus formation was encountered. The remains of the mastoid

cortex were removed with a curette, revealing a necrotic process which had completely removed the cellular structures of the mastoid. The remainder of the zygomatic cells together with the perisinus cells, periantral cells, and tip cells were exenterated. The sinus plate and tegmen were cleaned. Antrostomy was performed, and the necrotic contents of the antrum removed. The fracture was found to enter the antrum and to continue through the inner table between the antrum and the sinus where an epidural abscess was uncapped exposing an area of dura about 1.5 cm. in diameter. The wound was cleansed with 1:1000 aqueous merthiolate solution. A spirally cut soft rubber tube drain was placed in the antrum and allowed to extend through the dependent portion of the mastoid incision. The incision was closed with interrupted No. 2 black silk sutures and mastoid dressing applied. The patient was returned to the ward in good condition.

Postoperative course was relatively uneventful. The patient was afebrile from the second postoperative day on. No discharge was ever present from the external auditory canal. Part of the sutures were removed on the fifth postoperative day. The remainder were removed on the sixth postoperative day. The post-auricular drain was left out on the twelfth postoperative day. On the seventeenth postoperative day the drum and post-auricular wound were both well healed. Audiogram done twenty-five days after surgery showed hearing to be normal and slightly better in the left ear than in the right. There has been no trouble with the left ear since.

Postoperatively 2,000,000 units of penicillin were given in doses of 20,000 units every three hours intramuscularly, together with a total of 38 grams of sulfadiazine in doses of 1 gram every six hours. Alkalinity was maintained with sodium bicarbonate, and fluid balance was carefully watched. Nasal shrinkage was elicited through the aid of ephedrine nose spray. Immediately after operation a transfusion of 500 c.c. type O whole blood was administered.

Postoperative roentgenograms were made to study the operative defect.

#### DISCUSSION

A direct blow on the mastoid, such as this patient experienced, of sufficient force to cause a fracture, may result in either immediate or delayed complications, or both. The immediate complications will depend upon the extent and direction of the fracture line and whether or not important structures are injured in its path. The thickness of the mastoid cortex and the type of development of the air cells, as well as the strength of the force applied and the

speed and size of the object causing the impact, will have a bearing on the direction and extent of the fracture, which will follow the path of least resistance. A thick cortex will obviously offer more resistance than a thin one, while a pneumatic mastoid will fracture more readily and more extensively than a sclerotic one. A rifle bullet, traveling at high speed, will penetrate the bone with very little or no shattering. On the other hand, a relatively large object, traveling at a slower speed, may produce a fracture line radiating in various directions. L. Bathe Rawling, cited by Wm. J. Mellinger,<sup>1</sup> claims that it will, in general, tend to pass through the outer cortex, jugular foramen, along the petro-occipital suture, and then through the body of the sphenoid. It may pass in other directions, such as the wall of the external auditory meatus, the mastoid antrum, the middle ear, the tegmen tympani, the inner mastoid cortex, the sinus plate, and longitudinally along the petrous pyramid, passing by or through the bony labyrinth and cochlea.

Important soft structures may be injured along the course of the bony defect. There will be local hemorrhage into the contiguous structures. The membrana tympani may be lacerated or ruptured, accompanied by hemorrhage through the external auditory meatus. The facial and auditory nerves, as well as the vagus or glossopharyngeal nerves, may be lacerated or infiltrated by edema or hemorrhage. The membranous labyrinth and the organ of Corti may be lacerated or may be the seat of hemorrhage, especially at the first turn of the cochlea. Vascular structures, such as the lateral sinus, jugular bulb, superior petrosal sinus, inferior petrosal sinus, or the carotid artery may be torn and cause serious hemorrhage.

This patient was fortunate enough to escape injury to important soft structures and organs. However, he illustrates the danger of delayed infectious complications. His fracture extended through the mastoid cells, both the inner and the outer cortex, the mastoid antrum, and the posterior bony

wall of the external auditory meatus. Thus the pathway for infection to spread was opened from beneath the external periosteum through the air cells and antrum to the epidural space. The injury itself, plus the accompanying hemorrhage into the cells, antrum and middle ear, resulted in an area of lowered local resistance. Therefore, the stage being set, with the advent of an acute upper respiratory infection five or six weeks later, it was a comparatively easy matter for the infection to invade the middle ear and spread along the prepared area, resulting in acute suppurative otitis media and mastoiditis, subperiosteal abscess and epidural abscess.

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### DICUMAROL

#### THE USE OF DICUMAROL IN THE PREVENTION AND TREATMENT OF INTRAVASCULAR CLOTTING AND EMBOLISM

SAMUEL A. ROMANO, M. D.†

NEW ORLEANS

The object of this paper is to discuss the use of dicumarol [3-3'-methylene-bis (4-hydroxycoumarin)] in the prevention and treatment of postoperative thromboembolism. Intravascular clotting has always been a serious problem both in medicine and in surgery. In recent years the increased number of operative procedures performed on patients in the older age group has made intravascular clotting an even more serious problem to the surgeon. Many measures are employed to reduce the incidence of this complication. Preoperative measures include the correction of fluid and electrolyte balance, removal of foci of infection, maintenance or reestablishment of normal cardiovascular function and correction of anemia or blood dyscrasias. During operation, prevention or correction of circulatory collapse and of dehydration, min-

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imal traumatization of tissue, and the avoidance of chilling are important considerations. In the postoperative state early ambulation, maintaining the patient in a Trendelenburg position until he can actively flex and extend the lower extremities, deep breathing, compression bandages applied to the extremities, active and passive movements of the lower extremities, and application of heat to the abdomen are measures used to decrease the incidence of postoperative thrombosis. In recent years vein interruption and anticoagulants have been advocated both as preventive and as therapeutic measures for intravascular clotting and embolism. The last two measures are the subjects of many articles in the current literature.

Femoral vein ligation decreases markedly the incidence of postoperative pulmonary embolism.<sup>1</sup> In patients with suppurative thrombosis, the treatment of choice is ligation of the vein proximal to the infected thrombus.<sup>2</sup> However, anticoagulants have produced such excellent results both in the prevention and in the treatment of bland thrombosis and embolism that the rationale of the added operative procedure necessary for vein ligation is questioned.<sup>3</sup> A comparison of the results obtained prophylactically with femoral vein ligation and with dicumarol therapy is given in table 1. Table 2 is

TABLE 1  
COMPARISON OF PROPHYLACTIC MEASURES  
AGAINST POSTOPERATIVE THROMBOEMBOLISM

	No. Cases	Venous Thrombosis	Fatal Embolism
Femoral Vein			
Ligation <sup>1</sup>	458	5 (1.1%)	1 (0.2%)
Dicumarol <sup>3</sup>	1,114	2 (0.2%)	0

a comparison of the results obtained with femoral vein interruption and dicumarol therapy in the treatment of postoperative thrombosis and non-fatal embolism. Figures quoted for vein interruption are taken from the last report of A. W. Allen and his group at Boston.<sup>1</sup> The figures given for dicumarol therapy are from the last report by E. V. Allen and his associates at the Mayo Clinic.<sup>3</sup> Of the 572 patients treated with dicumarol listed in table 2, 292 had non-fatal embolism

before treatment was started. Of these only 3 patients developed subsequent venous thrombosis and only 1 patient developed subsequently a fatal embolism.

TABLE 2  
RESULTS OF TREATMENT OF POSTOPERATIVE  
THROMBOSIS AND EMBOLISM

	No. Cases	Subsequent Thrombo- embolism	Subsequent Fatal Embolism
Femoral vein			
Ligation <sup>1</sup>	1,060	53 (5%)	5 (0.5%)
Dicumarol <sup>3</sup>	572	11 (1.8%)	1 (0.2%)

Comparable results using heparin as an anticoagulant are reported by Murray,<sup>4</sup> Jorpes<sup>5</sup> and others. In a control series of untreated non-fatal embolism, 19 per cent developed subsequent fatal embolism and 44 per cent subsequent venous thrombosis.<sup>6</sup>

Dicumarol and heparin are the anticoagulants currently available for clinical use. The advantages and disadvantages of the two drugs are listed in table 3. A disadvantage of both is that hemorrhage may result from their use.

TABLE 3  
ADVANTAGES AND DISADVANTAGES OF HEPARIN  
AND DICUMAROL

Heparin	Dicumarol
1. Can be administered without laboratory control.	1. Administration must be carefully controlled by laboratory tests.
2. Immediate effect on the blood.	2. Effect delayed 24-48 hours or longer.
3. Effect on blood lost within an hour after withdrawal.	3. Effect persists for two to ten days after withdrawal.
4. Can be given only parenterally.	4. Can be given only orally.
5. Is expensive.	5. Necessary dosage costs only a few cents a day.

#### MODE OF ACTION OF HEPARIN AND DICUMAROL

The exact mechanism of the anticoagulant effect of heparin is not known. According to Loewe and Hirsh<sup>7</sup> it prevents the formation of thromboplastin from platelets and acts both as an antiprothrombin and as an antithrombin. The exact mechanism of the action of dicumarol is unknown but its effect on the blood is a depression of the prothrombin concentration.

#### CONTRAINDICATIONS TO THE USE OF DICUMAROL

The following are considered contraindications to the use of dicumarol: (1) Bleed-

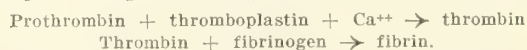
ing from any cause; (2) purpura of any type; (3) the presence of renal insufficiency; (4) the presence of jaundice if associated with prothrombin deficiency; (5) hepatic cirrhosis or hepatic insufficiency; (6) recent operations on the brain or cord; (7) subacute bacterial endocarditis. Dicumarol must be administered with caution in the presence of ulcerative lesions, of open wounds or of potential bleeding surfaces. Fever or toxemia enhances the action of the drug.

#### ADMINISTRATION OF DICUMAROL

The purpose of dicumarol therapy is to depress the prothrombin concentration to a level sufficiently low to prevent intravascular clotting and at the same time maintain a level high enough to prevent bleeding. To do this the prothrombin level should be maintained between 10 and 30 per cent of normal. Because of marked variation among different patients in sensitivity to dicumarol, dosage is an individual problem with each patient. Dicumarol should not be used unless daily and consistently comparable prothrombin determinations are available. Without such tests it is impossible to know if the prothrombin concentration is depressed sufficiently to prevent clotting or if it is so depressed that serious bleeding may occur. The total amount of drug to be administered in one day should be given in one dose.

#### DETERMINATION OF THE PROTHROMBIN LEVEL

Quick's method or one of its modifications is used for prothrombin determination. An understanding of the method employed to estimate prothrombin concentration and of the interpretation of the test is necessary for proper use of dicumarol. The present day conception of blood clotting may be expressed by the simple formula:



In Quick's test<sup>8</sup> all components necessary for clotting are present in excess except prothrombin. The test is performed as follows: 4.5 c.c. of blood is obtained by venepuncture and mixed with 0.5 c.c. of 0.1 molar sodium oxalate solution. The oxalated blood is then centrifuged at low

speed for a few minutes. One-tenth c.c. of plasma is added to 0.1 c.c. of thromboplastin solution in a test tube 100 x 13 mm. The thromboplastin can be prepared in the laboratory or a commercial preparation may be used. The plasma-thromboplastin mixture is placed in a water bath at 37.5° C. for one minute. Using a short serologic pipette 0.1 c.c. of 0.02 molar calcium chloride solution is forcibly blown into the plasma-thromboplastin mixture. The tube is rocked from side to side. The time required for the formation of a clot after the addition of the calcium chloride solution is the prothrombin time or the clotting time. A stop-watch is used to determine the number of seconds required for clotting. This test is repeated on serial dilutions of normal plasma with isotonic saline solution and the clotting times recorded on a graph. Figure 1 is a typical curve obtained with serial

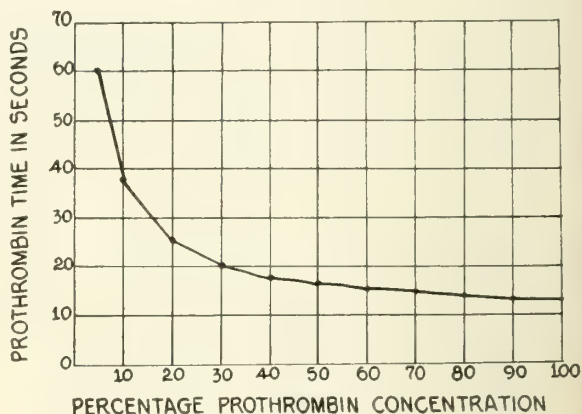


FIG. 1.

dilutions of normal plasma. The curve varies with the activity of the thromboplastin solution. Each new batch of thromboplastin must be standardized. Because thromboplastin solutions are unstable their activity should be frequently rechecked.

When the clotting time for an unknown plasma is obtained, the percentage of normal concentration of prothrombin can be determined by referring to the standardization curve. Prothrombin should be reported in per cent of normal concentration and



not in seconds. Figure 2 contains curves obtained with three different thromboplastin preparations. Reference to figure 2 reveals why it is dangerous and confusing to report prothrombin in seconds rather than in per cent of normal concentration. Forty seconds in Laboratory A represents 9 per cent normal concentration, in laboratory B, 30 per cent normal concentration, and in laboratory C, 18 per cent normal prothrombin concentration.

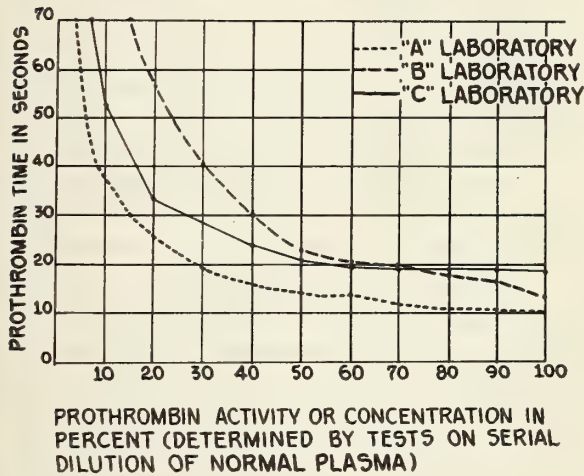


FIG. 2.

Bleeding occurs with prothrombin concentrations of 10 per cent or lower.<sup>8</sup> Between the levels of 10 and 30 per cent of normal, intravascular clotting is unlikely to occur.<sup>9</sup> In dicumarol therapy the prothrombin level should be maintained near 20 per cent of normal.

Modifications of Quick's original test such as the Magath<sup>10</sup> and the Link<sup>11</sup> modifications are quite satisfactory as a guide in dicumarol therapy. Smith's bedside modification<sup>12</sup> is not suitable. Russel's viper venom (stypven) has been used as a substitute for tissue thromboplastin in prothrombin determinations,<sup>13, 14</sup> It offers an advantage over thromboplastin from tissue extracts in that it is much more stable and with its use it is easier to determine the end-point in the weaker concentrations of prothrombin.

## THE DOSAGE OF DICUMAROL

For prophylaxis against thrombo-embolism dicumarol is started on the second post-operative day. Each day before dicumarol is administered, a prothrombin determination must be done. The following routine is recommended:<sup>6</sup> 300 mgm. of dicumarol is administered the first day; 200 mgm. dicumarol on the second day; 200 mgm. of dicumarol are administered each succeeding day that the prothrombin concentration is greater than 20 per cent. If prothrombin concentration is less than 20 per cent of normal, no dicumarol is given that day. If the prothrombin concentration is less than 20 per cent, but the level is rapidly rising, dicumarol may be administered; if the level has been rapidly falling even though the level is a little above 20 per cent dicumarol should be omitted that day. Figure 3 illustrates a typical prothrombin response to dicumarol and the method of adjusting the dosage.

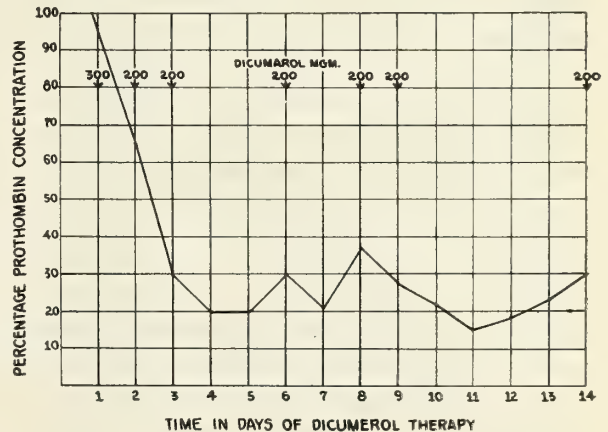


FIG. 3.

Prothrombin depression should be continued two to seven days after the patient is ambulatory. When prothrombin concentration returns to normal, there is no further protection against thrombosis. Previous administration of dicumarol has no effect on subsequent use of the drug. Patients have been carried with prothrombin levels between 10 and 30 per cent for as long as three months without any untoward effects.<sup>6</sup>

THE SIMULTANEOUS USE OF DICUMAROL AND  
HEPARIN

Because the effect of dicumarol after oral administration is delayed twenty-four to forty-eight hours or longer, heparin is given simultaneously with dicumarol when a rapid anticoagulant effect is desired. As soon as dicumarol depresses the prothrombin concentration sufficiently, heparin may be discontinued. When using both anticoagulants, blood samples for prothrombin determinations should be drawn two or three hours after the last dose of heparin to avoid the effect of heparin itself upon the clotting.

BLEEDING AS THE RESULT OF DICUMAROL  
THERAPY

In 1000 cases in which dicumarol was used, Barker<sup>6</sup> reports an incidence of 4 per cent of mild bleeding (mild epistaxis, microscopic hematuria, slight oozing from the wound), and a 2.5 per cent incidence of major bleeding (usually bleeding from the wound). All cases of major bleeding occurred in patients with a prothrombin concentration under 10 per cent of normal.

CONTROL OF BLEEDING DUE TO DICUMAROL  
THERAPY

If bleeding develops during the course of dicumarol therapy, repeated fresh blood transfusions and the intravenous administration of 64 milligrams of vitamin K should promptly control it. Stored blood rapidly loses its prothrombin concentration and is not suitable for use in this emergency. If an urgent operation is indicated in a patient receiving dicumarol the drug is stopped, large doses of vitamin K intravenously and fresh blood transfusions are given repeatedly until the prothrombin concentration reaches a safe level of 30 per cent or above.

## OTHER INDICATIONS FOR THE USE OF DICUMAROL

In addition to its use in postoperative thrombo-embolism, anticoagulant therapy has other uses in the field of surgery. It is useful after blood vessel anastomosis, after traumatic injury to vessels, and in sudden arterial occlusions. Its usefulness in chronic occlusive arterial disease has not been fully evaluated. In summary, when intravascular

clotting or embolism is a potential danger or has actually developed, anticoagulant therapy is indicated.

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THE Rh FACTOR IN CLINICAL OB-  
STETRICS AND GYNECOLOGY\*

J. W. DAVENPORT, JR., M. D.†

NEW ORLEANS

At the grave risk of being accused of making a deliberate understatement (which, of course, it is) I submit that Rh terminologies and genetic theories continue in a state of delightful uproar hardly calculated to soothe the professional ears of busy clin-

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icians or amuse them with various cabalistic symbols which jump around like fleas on a hot stove and at times make about as much sense.

If it please you, then, we shall try to ignore such distractions and consider Rh facts which are reasonably well established and of interest in relation to the cause and prevention of disease.

We can begin by glancing over the more familiar Rh landmarks, pausing here and there to meditate on the cussedness of nature in general and Rh in particular (for, indeed, until monkeys took to associating with people, blood banking was a pleasant career in nowise like the mad rushing about nowadays trying to get enough Rh— blood to go around!):

1. Relationship of Rh Factor to an agglutinin present in Rhesus monkey erythrocytes.<sup>1</sup>

2. Independent status of Rh relative to A, B, M, N, and other factors.<sup>2, 3</sup>

3. General incidence in white race: 85 per cent Rh+.<sup>2</sup>

4. High antigenicity in man.<sup>3</sup>

5. Absence of naturally occurring Rh antibodies in the blood.<sup>3</sup>

6. Relationship to hemolytic transfusion reactions.<sup>3</sup>

7. Relationship to hemolytic disease of the newborn (erythroblastosis fetalis, icterus gravis neonatorum, hydrops fetalis).<sup>3</sup>

8. Secretion of Rh antibodies in breast milk of isoimmunized mothers.<sup>4</sup>

9. Rh antigen demonstrable in certain organs and body fluids of some Rh+ people as well as in their erythrocytes.<sup>5, 6</sup>

10. Rh actually a complex or mosaic of closely related agglutinogens.<sup>7</sup>

11. The definite reciprocal relationship between the Rh Complex and the Hr Factor of Levine.<sup>7</sup>

Now let us consider the basic requirements for Rh isoimmunization. First, there must be a mechanism for antigenic transfer. This may take place by pregnancy and/or blood transfusion. Secondly, the donor (fetal) erythrocytes must possess an antigen absent from the red cells of the recipient (mother).

The rapidity and intensity of the response is controlled by individual antibody production, a widely variant property. About 50 per cent of all Rh— people are capable of sensitization if adequately exposed.<sup>12</sup>

#### Rh SUBFACTORS

The Rh Complex is comprised of three major subfactors, named in Wiener's present terminology Rh<sub>0</sub>, Rh' and Rh''.<sup>8</sup> These were identified by means of antisera of different specificities discovered in the bloods of various sensitized individuals, chiefly the mothers of erythroblastotic infants. The three antisera take their names from their specific antigens,<sup>8</sup> as shown in table 1.

TABLE 1

Rh agglutinogens	Rh <sub>0</sub>	Rh'	Rh''
Antibodies produced	anti-Rh <sub>0</sub>	anti-Rh'	anti-Rh''
Per cent + reactions (white)	85	70	30
Per cent — reactions (white)	15	30	70

Even as one may possess either the A or B factor or both of them, so do the Rh agglutinogens exist singly or in combination in the red cells of any given person. The absence of any one or more of these agglutinogens from the blood cells of an individual fulfills a basic requirement for isoimmunization.

The three most frequent combinations of Rh agglutinogens in the white race are as follows:<sup>8</sup>

	Per Cent
Rh <sub>0</sub> and Rh'	55
Rh <sub>0</sub> and Rh''	15
Rh <sub>0</sub> , Rh' and Rh''	15
The rare combinations are:	
Rh <sub>0</sub> alone	2
Rh' alone	1
Rh'' alone	0.5
Rh' and Rh''	0.01

Persons lacking all three of the agglutinogens are "true" Rh Negatives and comprise about 13 per cent of the white population.<sup>8</sup>

It is fortunate that the anti-Rh<sub>0</sub> (85 per cent) serum is the most frequently encountered. As Levine<sup>7</sup> states, this serum alone serves as a diagnostic reagent in 92 per cent of all cases of erythroblastosis, showing the father and affected infant to be Rh + and the mother Rh —. Similarly

it serves in diagnosing the Rh status in hemolytic transfusion reactions.

For practical purposes any patient whose blood fails to be agglutinated by anti-Rh<sub>0</sub> should be considered as “clinically” Rh — and so treated if in need of transfusion. Actually such person may belong to one of the rare subtypes such as Rh’ or Rh”. The important thing is to avoid administering blood containing an Rh factor absent from the blood of the recipient.

Rarely found alone, Rh’ and Rh” antibodies occasionally appear with anti-Rh<sub>0</sub> in the blood of a sensitized Rh— individual. A serum with anti-Rh<sub>0</sub> and anti-Rh’ has a specificity of 87 per cent, while anti-Rh<sub>0</sub> with anti-Rh” gives about 85.5 per cent positive reactions.

Rh ANTIBODIES

At present it is possible to identify two varieties or types of Rh antibody:

- 1. Simple immune antibodies (saline agglutinins)
  - a. Appear in early Rh sensitization.
  - b. Agglutinate Rh+ cells in saline (and other watery media<sup>9</sup>)
  - c. Are heat labile.
  - d. Tend to disappear from circulation in three months to two years.
- 2. Hyperimmune antibodies (\*)
  - a. Result from more prolonged isoimmunization.
  - b. Combine with (block) Rh+ cells in aqueous media without visible agglutination.
  - c. Are heat stable.
  - d. Visibly agglutinate Rh+ cells suspended in protein medium (plasma, serum albumin.)
  - e. Persist much longer than immune antibodies and usually replace them completely after a lapse of time following repeated exposures.

\*(Synonyms: Blocking,<sup>10</sup> incomplete,<sup>11</sup> coating,<sup>7</sup> albumin<sup>12</sup> antibody; conglutinin, glutinin.<sup>13</sup>)

Rh AND Hr

By means of the original anti-Rhesus or human anti-Rh<sub>0</sub> sera, white individuals were simply divided into Rh+ and Rh—.

Wiener’s original genetic theory held that the gene determining Rh+ was dominant over a gene determining Rh—, or absence of Rh<sup>2</sup>. Such is not the case, for while there is an absence of Rh agglutinin in Rh— cells there is actually another, reciprocally related agglutinin present.

This factor was first reported by Levine in 1942 following investigation of erythroblastosis in the infant of an Rh+ mother. In this and subsequent similar cases studied by Levine,<sup>7</sup> Race<sup>14</sup> and others the serologic picture was like this:

Father .....Rh+ or Rh—  
Mother .....Rh+  
Baby .....Rh+

Maternal sera showed atypical antibodies: against all Rh— bloods and various numbers of Rh+ bloods.

Since this newly discovered factor bore a striking reciprocal relationship with Rh, Levine named it Hr. It seems quite definite now that Hr is also a complex agglutinin and that there is a reciprocal Hr subfactor for each Rh subfactor. Factors Hr<sub>0</sub>, Hr’, and Hr” have been encountered.<sup>7, 12, 14</sup>

Like their Rh counterparts, Hr antibodies occur in both immune and hyperimmune forms. If one will think of Rh and Hr as single agglutinogens their relationship is clarified when its analogy to the M-N relationship, as first visualized by Levine,<sup>7</sup> is outlined as in table 2.

TABLE 2  
REACTION WITH ANTISERA

Type	Anti-M	Anti-N	(Genotype)
M+ (N—)	+	0	(MM)
(M—) N+	0	+	(NN)
M+ N+	+	+	(MN)

REACTION WITH ANTISERA

Type	Anti-Rh	Anti-Hr	(Genotype)
Rh+ (Hr—)	+	0	(RhRh)
(Rh—) Hr+	0	+	(HrHr)
Rh+ Hr+	+	+	(RhHr)

(Co-equal mendelian dominants. No recessivism.)

ABSTRACTS OF ILLUSTRATIVE CASES

CASE No. 1

Mrs. D. D., white, 26 years, para 2, grav 2. No prior history of transfusion.  
1942—Normal pregnancy and delivery. Child living and well.



1945—(October)—Hydropic female infant, expired two minutes after normal delivery. Pregnancy had been uneventful.

## SEROLOGIC STUDY

	Group	anti-Rh <sub>0</sub>	anti-Rh'	anti-Rh''	anti-Hr'
Father	0	+	+		0 (RhRh)
1st Child	0	+	+		+
2nd Child	0	+	+		+
Mother	0	0	0		+

Maternal serum: Rh agglutinins 1:64. Two days following delivery mother uneventfully received 500 cc. Group O, Rh— blood.

## CASE No. 2

Mrs. M. D., white, 30 years, para 3, grav 3. Two transfusions group compatible Rh— blood in November 1945.

1941—Normal pregnancy and delivery female infant. Living and well.

1942—Normal pregnancy and delivery male infant. Living and well.

1946—Normal pregnancy and delivery female infant. Living and well.

## SEROLOGIC STUDY

		anti-Rh <sub>0</sub>	anti-Rh'	anti-Rh''	anti-Hr'
Father	0	+	+	+	+
1st Child	0	+	+		
2nd Child	0	+	+		
3rd Child	0	+	+	0	+
Mother	0	0	0	0	+

Maternal serum: No evidence Rh antibodies on repeated tests during and after pregnancy.

## DISCUSSION

Case 1 is typical of Rh sensitization due to pregnancy. Since the husband is homozygous (RhRh) the prognosis for future pregnancies is very poor.

The second case was included for comparison with the first, to illustrate individual variation in antibody response. The first patient became so highly sensitized that she lost her second baby as a result, while the second patient had three normal Rh+ babies and showed no evidence of Rh antibodies in her blood.

## CASE No. 3

Mrs. L. E., white, 36 years, para 0, grav 1.

1945—Transfusion group compatible blood. No reaction. Rh unclassified.

1947—Induced labor 11 days following E.D.C. Delivered of macerated, stillborn fetus which had expired some six weeks earlier.

## SEROLOGIC STUDY

		anti-Rh <sub>0</sub>	anti-Rh'	
Husband	B	+	+	Rh+
Donor (1945)	A	+	+	Rh+
Patient	A	0	0	Rh—

Patient's serum:

Five months prior to E.D.C.—

Rh hyperimmune antibody ++

Six days after delivery—

Rh hyperimmune antibody +++++

## DISCUSSION

Here is what may result from disregarding the Rh type of a female patient in transfusion therapy. If this woman had been Rh typed and given Rh— blood there is little doubt that her baby would have been unaffected. This case, like numerous others previously reported,<sup>15, 16, 17, 18</sup> emphasizes the need for routinely Rh typing all female patients who are to receive transfusion.

## CASE No. 4

Mrs. J., 26 years, white, para 3, grav 3.

1938—Normal pregnancy and delivery. Female infant, living and well.

1940—Same.

1942—Transfusion 500 c.c. group compatible blood. No reaction.

1946—Normal pregnancy and delivery; female infant. Amniotic fluid and vernix dark yellow. Baby jaundiced in first 24 hours. Anemia. Recovered with transfusions of Rh— blood.

## SEROLOGIC STUDY

		anti-Rh <sub>0</sub>	anti-Rh'	
Father	0	+	+	Rh+ (RhHr)
1st Child	A	0	0	Rh— (HrHr)
2nd Child	0	+	+	Rh+ (RhHr)
3rd Child	A	+	+	Rh+ (RhHr)
Donor	A	+	+	Rh+
Mother	A	0	0	Rh— (HrHr)

Maternal Serum: Rh agglutinins +. Rh hyperimmune antibody +++++

## DISCUSSION

Here is an Rh sensitization due to transfusion and pregnancy combined. The father is heterozygous (since one of the children is Rh—), and prognosis for future pregnancies thereby somewhat improved. Again our attention is called to the potential dangers of ignoring the Rh types of female transfusion recipients.

## CASE No. 5

Mrs. B. T., 33 years, white, para 2, grav 2.

Pregnancies and deliveries had been normal. Both children living and well. Hospitalized May 1945 for cholecystectomy. Reported Group A Rh+ by

externe. Received 500 c.c. apparently compatible A Rh+ blood during operation. Shortly thereafter exhibited a temperature of 101° and pulse rate of 160. Marked jaundice appeared on second postoperative day. Palpebral edema. Urinary suppression was evident early, output being only 70 c.c. in first 24 hours. Urine dark red due to hemoglobin pigment. Urinary output gradually increased and patient recovered.

SEROLOGIC STUDY

	anti-Rh <sub>0</sub>	anti-Rh'	anti-Rh''	
Husband	+	+	+	(Rh <sub>0</sub> '')
Patient	0	0	0	Rh—(HrHr)
Patient's serum on third postoperative day:				
Rh <sub>0</sub> agglutinins: 1:64 +++++				
Rh'' agglutinins: ++				
(Children not available for testing.)				

DISCUSSION

Several interesting things are apparent in this case. First is the necessity for *accurate* Rh typing. Secondly, we perceive that ordinary cross-matching procedures may fail to detect Rh antibodies. Presumably one (or both) of the children is Rh+ and caused the primary sensitization. Here, also, we see an example of two different specificities of Rh antibody present in the same serum.

CASE No. 6

M. Y., 31 years, white, para 3, grav 3.  
1937—Normal pregnancy and delivery, male infant. Living and well.  
1942—Same. Due to excessive blood loss at delivery mother was given a series of five transfusions over a period of several days. The first was from the husband and there was no untoward reaction. Patient experienced chills and fever during third transfusion. Two subsequent transfusions were received uneventfully.  
1945—Normal pregnancy and delivery of male infant. Baby exhibited mild anemia and erythroblastemia on second day, but recovered without transfusion.

SEROLOGIC STUDY

	anti-Rh <sub>0</sub>	anti-Rh'	anti-Rh''	
Father	O N +	+	0	Rh <sub>0</sub> '
Baby	O N +	+	0	Rh <sub>0</sub> ' (RhHr)
Mother	O N 0	+	0	(Type Rh') Rh—
Maternal Serum: Rh <sub>0</sub> agglutinins 1:16. (First two children not available for testing.)				

DISCUSSION

As mentioned earlier 92 per cent of all cases of erythroblastosis are due to the Rh Factor as defined by the anti-Rh<sub>0</sub> (85 per

cent serum.) Of the other 8 per cent Rh subtype sensitizations account for a small number. Case number 6 is in point. Although the mother possessed the factor Rh', as did the father and baby, she lacked the Rh<sub>0</sub> component and hence could be sensitized to it.

Other rare sensitizations are due to the A or B factors and to the Hr factor and the concluding cases are examples.

CASE No. 7

Quadroon, 26 years, para 2, grav 2. No history of transfusion.  
Feb. 1945—Normal pregnancy and delivery. Infant expired on 7th day, cause unknown to patient.  
Mar. 1946 Normal pregnancy and delivery. The baby showed deep jaundice, erythroblastotic anemia, enlarged spleen on third day. Several transfusions of group compatible Rh+ blood were given. Infant expired on eighth day.

SEROLOGIC STUDY

		Antisera Rh <sub>0</sub>	Rh'	
Father	B	+	+	Rh+
Baby	B	+	+	Rh+
Mother	O	+	+	Rh+
Maternal Serum: No evidence Rh-Hr, M-N antibodies. Anti-A titer 1:128 (normal), anti-B titer 1:2048. No evidence B substance in serum of baby. Presumably a "non-secretor."				

CASE No. 8

I. L. G., quadroon, 26 years, para 4, grav 4.  
1938—Received "several transfusions" while hospitalized for surgical treatment of Paget's disease of the breast. Recalls no untoward reaction.  
1941—Normal pregnancy and delivery, female. Living and well.  
1943—Same.  
1945—Same.  
1946—Normal pregnancy and delivery, female. Intense icterus and erythroblastotic anemia early in neonatal life. Full recovery following several transfusions of group compatible blood.

SEROLOGIC STUDY

		Rh <sub>0</sub>	Rh'	Rh''	Hr'	
Father	O	+	0	0	+	Rh <sub>0</sub> (RhHr)
1st Child	A	+	+	0	+	Rh <sub>0</sub> ' (RhHr)
2nd Child	O	+	+	0	+	Rh <sub>0</sub> ' (RhHr)
4th Child	O	+	+	0	+	Rh <sub>0</sub> ' (RhHr)
Mother	A	+	+	0	0	Rh <sub>0</sub> ' (RhRh)
Serum: Rh <sub>0</sub> agglutinins: + (weak) Hr' hyperimmune antibody +++++						

The serum of this mother is undergoing intensive study in several laboratories. This case is to be presented in full detail later.<sup>19</sup>



## GENERAL COMMENT

Nobody wants to make laboratory technicians out of clinicians, yet the men responsible for ordering transfusions and for the welfare of their obstetric patients and unborn infants, should be generally conversant with technics if for no better reason than the encouragement of high standards in clinical laboratories. In the earlier days of Rh, with incomplete knowledge of the problem and reliable Rh testing sera almost unobtainable, bizarre and uncertain results were frequently popping up. (I popped up a good number myself).

The passage of only a few years has made such things inexcusable in view of our present knowledge of Rh and the fact that reliable testing sera are available from several sources. Yet a casual approach to the Rh problem, especially Rh typing, seems all too prevalent. Specifically I condemn the following:

1. The tendency to rely on a single anti-Rh<sub>0</sub> testing serum, a condition aggravated by the not yet extinct custom of turning someone loose with a serum labeled anti-Rh without adequate instruction for accurate Rh typing and no concern about any kind of controls.

2. Failure to employ routinely two or more of several efficient Rh typing technics, thereby eliminating another effective control check on results.

3. The use of dirty glassware.

4. Neglect of even rudimentary aseptic technic in handling Rh antisera.

5. Improperly labeled blood samples or samples not labeled at all and identified by guess and by God.

Well, you might say, why does this fellow speak thus? I am sure you know the answer lies in the protection due your patients, protection against hemolytic reactions, against the antibodies which can destroy their unborn babies. The fact that some transient carelessness in a laboratory can rob a child of life before he sees the light of day should be answer enough.

Having unburdened my soul, I beg leave to visit your domain. It usually happens that a newly launched citizen becomes "the

pediatrician's baby" and our colleague assumes the burden of seeing that his small patient receives any necessary transfusions. It is well established that erythroblastotic babies of Rh— mothers respond best to transfusions of antibody free Rh— blood. This is chiefly due to the fact that maternal antibodies remain in the infant's circulation for varying periods of time following birth and will destroy transfused Rh+ red cells even as they destroy the baby's erythrocytes. This does not help baby any.

Our most promising therapeutic weapon at present is the replacement transfusion, an old idea modified to bring about removal of the infant's blood with constant substitution of suitable Rh— donor blood. This treatment seems of especial value in those infants in whose circulations maternal hyperimmune (blocking) antibodies are present. Diamond,<sup>20</sup> using a small plastic catheter inserted in the umbilical vein, reports exceptional results in nearly 40 babies so treated. There is some reason to believe that even a partial replacement transfusion is of value in these cases.<sup>21</sup> Premature delivery, by induction or section, while theoretically beneficial in removing the baby from a harmful environment, has not seemed to confer any real advantage, and has several obvious disadvantages.

The obstetrician and gynecologist are key figures in the Rh problem. They can rightly demand and enforce routine Rh typing of all their patients, regardless of age or marital status so that no Rh— female patient will be exposed to possible sensitization by transfusion. In this connection it must be remembered that 5 or 10 c.c. of Rh+ blood injected into the buttock of an Rh— baby girl is no less a potential danger than the administration of the same blood by vein.

Prevention of pregnancy Rh immunization is a problem of a different sort, approached by some with suggestions that premarital Rh typing be required by law and by others who advocate artificial insemination. To me these are but make-shifts until such time as the biochemists provide us with a non-antigenic fraction of

the Rh molecule for the *in vivo* neutralization of antibodies in pregnant women. The development of this agent is well within the realms of probability.

#### SUMMARY

An Rh evaluation on each obstetric patient should become a part of modern prenatal care. The following routine is suggested:

1. Transfusion history, with names and addresses of donors, if known.
2. Routine Rh typing.
  - (a). Especially for multigravidae and for primagravidae having history of blood transfusion.
3. Rh type husband.
  - (a). When wife is Rh—
  - (b). When wife is Rh+ but has history suggesting possible isoimmunization.
4. Rh typing of children.
  - (a). Only when definitely necessary.
5. Rh and/or Hr antibody tests.
  - (a). When husband is Rh+ and wife Rh—
  - (b). When husband is Rh—and wife is Rh+.
  - (c). When both husband and wife are Rh+, but wife's history suggests possible isoimmunization.
  - (d). Schedule of antibody tests
    - (1) During third or fourth month.
    - (2) Repeat in sixth, seventh and eighth months.
  - (e). Interpretation of antibody tests
    - (1) If remain negative in eighth month, prognosis is excellent. Indicates absence of isoimmunization.
    - (2) Antibodies appearing three months or less before term usually indicate possibility of a mild hemolytic disease, with ultimate prognosis good.
    - (3) Earlier appearance of antibodies increases unfavorable prognosis.

- (4) Titer of antibodies of no constant practical significance.

(a) Type of antibody is important since a more serious prognosis is reflected by presence of hyperimmune antibodies.

- (5) *Presence of antibodies at any time is not conclusive evidence that baby will be affected.*

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Davenport has given an excellent, complete presentation of the subject of the Rh factor and I do not feel that I can add anything to his presentation. However, I may call attention to two important remarks which he made in closing: First, that every pregnant woman, in addition to the usual blood grouping, should have her blood examined to determine whether she is Rh positive or Rh negative and second, that no girl or woman who may or may not have reached the childbearing period should have a transfusion without having had her blood tested for the Rh as well as the usual grouping and cross matching.

## HEMATURIA\*

### ITS CLINICAL SIGNIFICANCE

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In presenting this subject for consideration, no attempt will be made to present anything new or unusual regarding hematuria. There is an abundance of medical literature dealing with this important symptom, and all modern text books of urology emphasize its potential seriousness and usually provide a rather full discussion of its causes and treatment.

Nevertheless, we feel that the subject of hematuria is of such importance to the medical profession that it deserves a place on the agenda of a general meeting, even at the risk of the repetition of facts and statistics drilled into us as students and internes, and gleaned from our medical journals.

At this time it is probably well to take a few moments to discuss briefly the types of hematuria recognized. Hematuria is classified as gross or microscopic. In an attempt to localize the portion of the genito-urinary tract from which it arises, it is further described as initial, terminal, or total.

In initial hematuria, blood is present only in the first part of the specimen voided. Lesions distal to the internal sphincter muscle are commonly responsible for initial hematuria. Less often the bleeding is present between urinations and blood flows from the urethra and its origin is distal to

the external sphincter. Examples of the latter type are trauma to the urethra and new growths.

Terminal hematuria exists when blood is present in the last portion of the voided specimen with the first part clear. Lesions of the prostate, posterior urethra, and bladder are responsible for this type of hematuria. In these instances the trigon, assisted by the perineal, and other accessory muscles of urination, squeeze blood out of a congested or ulcerated lesion or from a bladder tumor.

Total hematuria denotes blood uniformly distributed throughout urination. It is most often due to lesions of the bladder, or one, or both kidneys. It must always be kept in mind that this evidence is insufficient to localize the lesion and rarely defines the pathology responsible for the hematuria.

The following etiologic tabulation, as used by Hinman, emphasizes the most important causes of hematuria, but is by no means exhaustive. However, it readily points out the detailed study necessary at times to elicit the true factor responsible for blood in the urine.

#### I. General Causes (extra-urinary).

##### A. Blood Dyscrasias:

Hemophilia, erythremia, scurvy, morbus maculosus, purpura, jaundice, leukemia, Hodgkin's disease, etc.

##### B. Infections:

###### 1. Infectious fevers:

Typhoid, malaria, smallpox, scarlet fever.

###### 2. Local infections adjacent to the tract:

Appendicitis, pelvic abscess, perinephritis.

##### C. Medicinal or toxic:

Cantharides, turpentine, urotropin, sulfonamides, dicoumarol.

##### D. Nervous:

Tabes dorsalis, vicarious menstruation, hysteria.

#### II. Local Causes (urogenital).

##### A. Lower tract:

###### 1. Urethra (initial hematuria is the

\*Read before the sixty-seventh meeting of the Louisiana State Medical Society, May 13-15, 1947.

rule, i.e., blood at the beginning of urination).

Particularly posterior urethral infections.

Stricture.

Foreign bodies or trauma.

Prostatic conditions.

Tumors.

2. Trigone and neck of the bladder.  
(Terminal hematuria is the rule, i.e., blood at the end of urination).

#### B. Midtract:

Stone,

Tumors of the bladder cause at least 50 per

1. Bladder cent of all massive hematurias (Herman),  
Ulcer and infections,  
Diverticulum,  
Trauma.

#### C. Upper tract:

Stone,

1. Ureter Stricture,  
Tumor,  
Trauma.

The five most frequent causes are:

1. Stone
2. Renal Tumors,
2. Kidney 3. Tuberculosis,  
4 Infection,  
5. Glomerulonephritis.

But any disease of the kidney may cause hematuria.

In the presence of hematuria, two questions immediately present themselves for solution. What is the source of the bleeding? What pathologic process is responsible? Bleeding from any source of the body always alarms the patient and it is not surprising that when gross bleeding from the urinary tract occurs, the patient usually seeks medical aid. Unfortunately, the physician may not share his alarm; reassures the patient and some form of drug is ordered. Cessation of the bleeding nearly always occurs and the patient gets a false sense of security. We must always remem-

ber that practically all urinary tract bleeding is intermittent and that cessation in no way indicates cure, or the degree of seriousness. Other factors are frequently present, which cause a delay in proper investigation. These are the excellent general health of the patient at the time of his first spell of bleeding, and the frequent absence of pain, chills or fever, and loss of weight. In instances of microscopic hematuria, without concomitant symptoms of pain, fever and so on, greater delay in securing medical advice and proper investigation usually occurs with consequent increase in morbidity.

#### INCIDENCE

I would next like to present some statistics regarding hematuria, to emphasize its importance. In 99 consecutive cases, Kretchmer found that 96 per cent of hematurias had their origin in the urinary tract, and that only 4 per cent were due to extra-urinary causes. Ravich reviewed from his office practice, a total of 2,246 cases from the years 1916 to 1935, in which a definite diagnosis was made with the following results: (1) In 50 per cent of all cases of hematuria, stone somewhere in the urinary tract, was the responsible factor. (2) Stone was also the etiologic agent in 50 per cent of all cases of gross hematuria. (3) Tumors of the urinary tract were responsible for 240 of the 2,246 cases, or roughly, 10 per cent; and in one out of five of all cases of frank hematuria, or 20 per cent. (4) Nephritis, a very common diagnosis made, was responsible in only 2 per cent of the series. Hospital statistics also confirm the seriousness of hematuria as a symptom, and are added evidence that its source and cause should be ascertained promptly in all cases. In 1932, MacKenzie reported a study of hematuria from the Royal Victoria Hospital. In 20 per cent of all urologic admissions, blood was present in the urine and in 75 per cent of the cases, the hematuria was caused by one of four lesions—tumor, infection, stone, or nephritis. Ewell states that, "50 per cent of all massive hematurias are due to tumors of the bladder." Of 902 cases of bladder tumors reported by the Carci-



noma Registry of American Urologic Association, the initial symptom was hematuria in 63.9 per cent. Approximately 60 per cent of all hematurias are from the lower genito-urinary tract and 40 per cent from the upper. It can be seen from the above statistics, that the most prevalent causes of hematuria, namely, tumor, infection, stone, and nephritis, are all serious lesions and demand complete study and prompt attention.

While the incidence of hematuria in general practice is not very great, we must realize that the family physician is the individual to whom patients go for advice in these matters. Consequently, if thorough investigation is to be promptly secured, it is necessary that the physician be convinced of the following: (a) Seriousness of hematuria; (b) that the bleeding will usually stop, with or without medication, and that it may not recur for months or even a year; (c) that besides careful routine physical examination and laboratory studies, cystoscopy and pyelograms are usually required to localize the lesion; (d) while urologic studies occasionally require repetition, they are in nearly all cases conclusive. This brings up the question of—is it important to examine patients while bleeding and why? The answer to the urologist, of course, is—yes. It must be puzzling to someone not familiar with cystoscopy and pyelography, to be told that a lesion of such gravity as to cause gross bleeding, frequently can not be detected very readily by careful observation in a few days to a week after the bleeding has subsided, yet this is seen repeatedly.

A small stone in the lower ureter may be passed incorporated in a blood clot and not be seen by the patient. An infection responsible for acute hemorrhagic cystitis may spontaneously subside within a week. Gross hematuria from one kidney, which could have been readily detected on cystoscopy, may, a few days later, require detailed exhaustive study and repeated pyelograms before a correct conclusion is arrived at. Consequently, it is obvious that we should, when at all possible, advise and encourage our patients to have prompt investigation

while bleeding, and to avoid delay by withholding medication, except where needed for the relief of pain or the control of an acute infection of the urinary tract.

Perhaps we, as urologists, have not kept the profession fully cognizant of the advances made in the technical side of diagnostic work in the past few years. Cystoscopic examination need not be associated with great discomfort and danger of reaction, as occurred too often in the past. The introduction of smaller instruments with good vision, the use of sulfonamides and penicillin, prophylactically and post cystoscopically, together with the use of small catheters, have made these examinations immeasurably safer. The use of intravenous anesthesia in hospital practice, and of demerol intravenously, in selected office urology, has also removed much of the apprehension and pain of the examination.

Before concluding the discussion, I would like to call your attention to two types of cases, which frequently confuse the physician in dealing with a complaint of hematuria. The first are those cases of rectal or vaginal bleeding present with hematuria—especially, painless variety. In these cases both patient and doctor may easily overlook the fact that the bleeding is also from the urinary tract. In women, catheterization is often necessary to prevent error. The second group of cases is much more difficult to diagnose accurately. I refer to the elderly male with symptoms and findings of benign hypertrophy of the prostate and in whom there also exists bladder tumor. In these cases gross hematuria is common, and the physician is apt to readily explain it on the basis of prostatic varices, and feel that no further examination is demanded, particularly if the bleeding subsides and the obstructive symptoms are minimal. Correct diagnosis can only be made by cystoscopic examination.

#### CASE NO. 1

J. M., a white male, aged 65, reported to his family physician in November, 1946, with a history of bloody urine of one week's duration. Blood was present on nearly each voiding and a few clots had been passed. For several years prior to this visit,

he had noted some difficulty in starting the stream and a mild nocturia. The patient was told that his prostate was enlarged, and that the bleeding was due to ruptured veins in the prostate gland. The gross bleeding subsided on rest and some oral medication. The gross bleeding did not recur until March 10, 1947, after a prolonged horseback ride, and was profuse. Two days later a cystoscopic examination revealed a rather large median lobe of the prostate causing obstruction at the bladder neck, but of much more importance, a large papillary new growth covering the left half of the trigone and still bleeding slightly. Fortunately, the biopsy was reported grade I carcinoma, and a resection of the prostate and the new growth was done one week later.

## CASE NO. 2

O. S., a white male, 45 years of age, was seen by his physician for a "check up" because he was not feeling well, but had no specific complaint related to any of the systems. A routine examination was essentially normal, except for persistent microscopic hematuria. The patient was advised of the hematuria and was told that possibly a silent stone was present, and an intravenous urogram was done. This was also normal and no further studies were made. The patient continued to work as a construction engineer until four months later, when frank hematuria developed while at work. He was promptly referred for urologic study and a papillary tumor,  $2\frac{1}{2}$  cm. in diameter, was found on the posterior wall of the bladder.

This case is presented to emphasize that hematuria in nearly all cases may require complete urologic study and that negative intravenous urograms, if not followed up by cystoscopy and other urologic studies will fail to determine the cause of many cases of hematuria. This is especially true in the cases of painless microscopic hematuria.

## CONCLUSIONS

1. Hematuria is not a clinical entity. It is a symptom which demands complete investigation and prompt diagnosis. The principal causes of hematuria of the urinary tract are tumor, stone, infection, and nephritis.

2. The majority of hematurias are due to intrinsic diseases of the urinary tract, but systemic diseases may also be the cause of hematuria.

3. Early determination of the pathologic lesion responsible for the hematuria is essential for a good prognosis.

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## DISCUSSION

Dr. Pratt: I do not know that I can say anything more than what Dr. Frederick has already said. Blood in the urine is to the urologist like waving a red flag in front of a bull. And it makes no matter where the bleeding comes from. If you, for instance, wash out a bladder, and then it washes clear and you have no blood, you cannot say that it is not coming from the bladder alone. I have seen some strange cases.

I have seen one patient—a lady—who came in with a hematuria. Cystoscopically we determined it came from the right kidney. Pyelograms were made and everything was normal. At regular intervals she would have bleeding from her right kidney, and we pyelogramed her about fifteen times in a period of about five years, and could never prove any pathology in that kidney. Well, after about seven years of Humes' and my treatment of just watching her, she got tired of being cystoscoped and pyelogramed, so she went to another doctor who removed the right kidney and then she started bleeding from her left kidney. I think she lasted about four or five days after that, and she had these spells of kidney bleeding. We could never prove any pathology in the kidney, and when they took out the one that was bleeding, and the other one started bleeding, I asked the other urologist, "Now, is she bleeding from the other side?" He said, "Yes, she is."

Symptomless hematuria: That is hematuria without any signs except blood in the urine. It demands a very close examination to determine whether or not you are dealing with a neoplasm. When a person comes into my office, bleeding, the first thing I think of is neoplasm because it is the worst thing the patient can have. I try to rule neoplasms out the very first thing, and if there is any suggestion of a neoplasm there I will have to check and recheck, and then if it shows up—because often blocking the pelvis of the kidney or one of the pelvises gives you a poor effect and I would rather do my cystoscopy and pyelograms when the patient is not in a bleeding spell.

We have seen more and more tumors of the kidney in the renal pelvis. I had, a couple of years ago, a man to come in with a symptomless hematuria, and he had a papillary growth of the pelvis of the kidney. I took the kidney out, and the ureter down to within two inches of the bladder, and I split the ureter open and there was no plants in



the ureter. A year later I looked in his bladder and I saw a little tumor sticking out of his bladder, and I had to go back, take out a piece of bladder and the stump of that ureter. I did it very peculiarly. It was rather bound down, following the first operation. I put a groove directly with the wall up through the ureter and tied it, and turned it inside out like you would a glove finger, and I took an area about that big (indicating) out around that.

Dr. S. S. Hargrove (Baton Rouge): I would like to say a word about one thing that the doctor mentioned, and that is on the occurrence of hematuria. In my territory dituperol is coming into more general use than it has been. One patient had a very gross hematuria that in the first three days knocked his blood count down to a million and a half. It did clear up. I think the profession might realize that dituperol might cause some serious hematuria.

Dr. John Menville (New Orleans): Of particular interest is the idiopathic type of hematuria. It is important that no renal surgery be attempted unless there is a demonstrable lesion; one exception is hemorrhage which endangers the life of the patient. Patients with hematuria should be checked at regular intervals until a definite diagnosis can be made. Intravenous urograms are reliable only when the outlines are clear cut and definite.

The interpretation of microscopic hematuria is sometimes a moot point. An occasional transient finding of microscopic blood in the urine, in the absence of any clinical findings, is not necessarily significant, but repeated microscopic blood in the urine warrants a complete investigation.

—o—

## THE MANAGEMENT OF PROSTATISM\*

U. S. HARGROVE, M. D.

BATON ROUGE

Although remarkable progress has been made, and is being made, in nearly all the fields of medicine and surgery, I do not need to remind you, the practicing physicians of Louisiana, that the millennium has not yet arrived in the practice of medicine. The layman is apt to get the idea, from reading the current magazines and newspapers, that wonderful science has discovered and perfected a cure for practically every disease, and that there is no excuse for a doctor's failure promptly to put a pa-

tient right on his feet, and without too much delay. The doctor, however, knows only too well that there are still innumerable headaches in this business, and that there are still many thorns to be found with the rose.

In spite of the truly remarkable progress made in recent years in the treatment of prostatism, unfortunately there are still plenty of headaches associated therewith.

Prostatism may be defined as a morbid or pathologic state due to disease of the prostate gland, chiefly those conditions of the gland causing obstruction to the urinary flow. In this paper, only those conditions causing obstruction will be considered.

### SYMPTOMS

The diagnosis of prostatism is relatively simple, but it is surprising how many patients are seen in consultation for supposed prostatism whose symptoms are due to some other condition. The condition most often mistaken for prostatism is stricture of the urethra.

The usual symptoms of prostatism are well known and can be listed about as follows:

1. Frequent urination—varying from three times night and day to every 15 minutes night and day.

2. Straining—varying from slight to very severe. As a sequel to this straining, many chronic prostatitis are found to have inguinal herniae on one or both sides, and aggravated hemorrhoids.

3. Weak stream. This symptom is the most constant of all the symptoms of prostatism, all patients having it, although it may have been so gradual in its progress that the man has forgotten what a good stream is like and may tell the doctor that his stream is all right.

4. Urgency. This may be slight to severe, and cause considerable embarrassment.

5. Dribbling at end of urination. This is the chief cause of wet feet in prostatitis.

6. Hematuria. This is not a common symptom, but it will often bring the patient to the doctor when other symptoms fail. No conclusion should be drawn about the

\*Presented at the Sixty-Seventh Annual Meeting of the Louisiana State Medical Society, May 14, 1947.

cause of the bleeding until after a thorough urologic examination has been made.

7. *Acute retention.* This is the symptom that always brings the patient to the doctor. Acute retention in an old man is almost, but not quite always, due to prostatism.

8. *Dysuria.* This term includes discomfort, burning, stinging, and painful urination.

#### EXAMINATION AND DIAGNOSIS

The examination of the patient suspected of prostatism should proceed as follows:

1. *A general examination*, including a survey of the cardiovascular system and a Wassermann test should be done. This should also include elicitation of the reflexes, especially the knee jerks and the pupillary reflexes, as the same symptoms caused by prostatism may also be caused by lesions of the central nervous system, notably *tabes dorsalis*.

2. *A urinalysis* is done, and should include observation of the act of urinating if the patient is able to cooperate. A large number of prostatics will show pus in the urine, varying from a few pus cells to a grade 4 pus content. Albumen is likewise often present, and also sugar.

3. *Digital examination* of the prostate is then done. Too much information is not gained by this examination, as an advanced degree of prostatism may accompany a small prostate, and a very large gland may, on the other hand, produce no obstructive symptoms whatsoever. The digital examination is most important in relation to the possible presence of a malignant tumor of the gland. This is the chief means of diagnosis of carcinoma of the prostate. A frankly malignant gland has a very characteristic feel to the index finger, and as most carcinomas start in the posterior lobe, the digital palpation of this lobe is very important.

4. *Palpation of the abdomen* is then in order. The greatly distended bladder may usually be palpated as a large rounded suprapubic mass. However in the absence of such a palpable mass, no conclusion should be drawn as to the presence or absence of residual urine.

5. *Examination of the external genitalia* for the common lesions of these organs is then carried out, followed by passage of a catheter into the bladder. I will admit that catheterizing a previously unmolested bladder is not without some possible dangers, but so much depends on the information thus gained that the advantages of catheterization far outweigh the disadvantages in my opinion. An aseptic technic should be strictly followed. If the bladder is greatly distended so that it is easily palpable as a rounded tumor mass rising above the symphysis, it is safer not to empty the bladder completely. The easily palpable distended bladder will usually be found to contain 32 oz. or more of urine. Enough can be drawn off through the catheter accurately to establish the diagnosis of distended bladder, by noting the disappearance or reduction in size of the suprapubic swelling, and the catheter can then be withdrawn, leaving the bladder decompressed but not empty. Some authorities claim that there is never any danger in completely emptying a chronically distended bladder, but this just is not so in my opinion. If the bladder is completely emptied, it is better partially to refill it with a mild antiseptic solution such as boric acid.

If a catheter is to be left in place for continuous drainage, a clamp should be applied to the catheter, and the clamp loosened at intervals so as gradually to decompress and empty the bladder. The patient at this time should be put on a urinary antiseptic. This will aid in the prevention of a sudden flare-up if infection is already present, and will assist in preventing infection if none is present to start with. Of course the particular urinary antiseptic indicated will depend on the type of infecting organism present in these cases already infected, but until this information is known, the best bet is to give two 7 1/2 gr. tablets of either sulfathiazole or sulfadiazine at the first dose, and then one tablet three to six times per 24 hours thereafter for the time being.

There are a few simple but important points in relation to catheterizing a prostatic that I wish to bring to your attention.



Every physician who may have to treat a prostatic in acute retention should have a number 14 or 16 French olive tipped coude catheter in his bag. This catheter has a curved tip which will usually ride over a hypertrophied middle lobe and on into the bladder, whereas a straight catheter will frequently impinge against the middle lobe and fail to enter the bladder. Much time is lost then, and much trauma produced trying different catheters, filliforms, or sounds, increasing the pain and shock and producing often considerable bleeding.

Gentleness should be stressed in these manipulations. The urethra should be accorded the same respect that is accorded the eye or any other sensitive organ. If the bladder cannot be entered after a reasonable trial, further efforts in this direction should be discontinued and consultation secured, or the patient hospitalized if not already in the hospital. If catheterization is then still unsuccessful, some type of suprapubic drainage will be required.

The further examination of the patient then consists of either cystoscopic visualization of the prostate and bladder, or x-ray visualization of these organs. Some urologists prefer one method, some the other, and some both. Intravenous pyelography is exceedingly helpful in working up a prostate case. The condition of the upper urinary tract is ascertained, and much information is gained as to the size of the prostate by making a film of the bladder region after most of the dye has passed into the bladder. By getting intravenous pyelograms, one is saved the embarrassment of overlooking some gross lesion of one or both kidneys as well as such conditions as diverticulum of the bladder, tumor of the bladder, and stone in the bladder. Both x-ray visualization and cystoscopic study are desirable, thereby getting all the information needed, and avoiding as far as possible a slip up in the diagnosis.

#### DIFFERENTIAL DIAGNOSIS

The diagnosis of prostatism is by now pretty well established. In the differential diagnosis, there are only a few conditions which may cause confusion. As stated

above, the most common mistake is made in case of stricture of the urethra in a man in the prostatic age. The symptoms of these two conditions are practically identical. However, during the course of the examination outlined above, the presence of the stricture will have been determined. Of course both conditions may coexist, but this must not be very common. Other conditions to be considered in the differential diagnosis are : (1) stone in the bladder ; (2) neurogenic bladder ; (3) tumor of the bladder ; (4) diverticulum of the bladder, and (5) a few other rare conditions. Under this last division, I have a patient at the present time who has a bony tumor of the sacrum which has reached such an enormous size that it has compressed the urethra up against the arch of the symphysis, causing complete occlusion of the channel, and producing all the symptoms of prostatism up to total retention.

Along with establishing the diagnosis of prostatism, the benign or malignant nature of the gland has also probably been ascertained. This differentiation is usually easy in the typical cases, but there are a fair number in which it is difficult to decide whether or not the gland is the seat of malignant changes. The benign and malignant may coexist. Digital palpation, cystograms, x-rays of the bony structure for metastases, and the phosphatase tests will all be used in making a decision. It is well to remember that statistics seem to show that about 15 or 20 per cent of prostatics have cancer of the prostate.

1. A bladder calculus may cause symptoms similar to prostatism. One important differential point is that stone in the bladder produces the most discomfort in the daytime, when the patient is up and about, while prostatism produces the most discomfort at night. The diagnosis of stone is readily confirmed by x-ray, cystoscopy, or both.

2. Neurogenic bladder may prove difficult of diagnosis. A distended bladder which is painless, and which seems to have no expulsive force when a catheter is passed, should excite suspicion of an atonic

type of neurogenic bladder. If the pupillary reflexes or knee jerks are absent, tabes will naturally be suspected, and investigated by spinal fluid examination. Recent opinions point to the probability that most neurogenic bladders are markedly influenced by mechanical factors at the bladder neck, chiefly prostatic obstruction. The prostate may offer just enough resistance to a weakened detrusor muscle to cause chronic urinary retention. The ultimate diagnosis in these cases may rest upon the interpretation of cystometrograms, along with the other findings.

3. Tumors of the bladder also may produce symptoms similar to prostatism, such as hematuria, frequency, straining, and dysuria. Here the only sure method of diagnosis is cystoscopic examination, although a cystogram is either diagnostic or suggestive in most cases.

4. A large diverticulum of the bladder may produce a foul urine, as well as the usual symptoms of prostatism. Diverticula are not usually suspected from symptomatology alone, but are found on cystogram x-ray films and on cystoscopic examination. They are most frequently present as a complication of bladder neck obstruction, due to prolonged back pressure against the bladder wall.

5. Of the various conditions which need to be differentiated from prostatism, stricture of the urethra is the most readily diagnosed, and should be picked up by the general practitioner without difficulty and without extensive instrumental and x-ray examination.

#### TYPE OF GLAND

It is not practicable for one other than the urologist to determine what type of obstructive gland is present. Whereas the greatly enlarged gland can usually be apprehended by a simple digital rectal examination, it is entirely possible for large intravesical lobes to be present without any gross enlargement being noticeable to the examining finger. Likewise, complete retention may be caused by a median bar, which can only be diagnosed cystoscopically. The type of enlargement moreover is of

interest chiefly to the operating surgeon, as he will, in most cases, take this into account in planning the type of operation to be performed.

#### TREATMENT

This brings us up to the subject of treatment. This subject can well be divided into non-operative, and operative treatment.

*Non-operative.* Many cases of prostatism can and should be treated by non-operative methods. Let me say here, that endocrine treatment has no place at the present time in the treatment of the benign prostate, both androgens and estrogens having failed to give any predictable results. The mild prostatic, whose chief complaints are a weakening stream and moderate nocturia, does not need to be rushed to the operating room unless at least several ounces of residual urine are present. If pyuria is present, local treatment consisting of bladder irrigations with a mild antiseptic solution, bladder instillations of 5 per cent argyrol, and some urinary antiseptic by mouth should be prescribed. If the gland is large and soft, or if the expressed secretion contains much pus, gentle prostatic massage will often give very definite results. If the gland is quite firm, it has been my experience that massage is of no benefit. Even if all the symptoms and findings of prostatism are present, including retention of urine, there are still some cases in which non-operative treatment is indicated, namely, patients who, because of advanced debility, serious cardiac lesions, or other third degree pathologic changes, have a life expectancy of only a few weeks or months at the best. Execution of these patients on account of inability to urinate is not good judgment. Catheter life is not pleasant, but it is better than no life at all. If catheterization is impossible, a quick suprapubic cystostomy under local anesthesia, or the introduction of a small catheter using a trocar suprapubically should be the treatment adopted.

Thus the mild prostatic and the advanced prostatic with a short life expectancy due to other pathological changes, are elimi-



nated from the list of candidates for prostatectomy.

*Operative treatment.* The patient who has a reasonable life expectancy, and who has moderate or severe symptoms and findings of prostatism, should be advised to have his prostate operated upon. At this point, the general or family physician, or medical advisor, should refer the patient to a competent urologist. The referring physician should not attempt to select the type of operation to be performed, but should leave that strictly to the operating surgeon. There are, as you well know, the transurethral, the suprapubic, and the perineal methods of relieving the prostatic obstruction. Each method has its good points, and bad points, and the choice of method should be left to the discretion of the man who does the operation. If the operation to be performed is determined by anyone other than the operating surgeon, undesirable results may ensue. Suffice it to say here that all the three methods are capable of giving good results, and all are likewise capable of giving poor results, and the judgment of the urologist should be accepted by the patient and by his referring physician, as to which operation is to be done. The operator should likewise be responsible for choice of anesthetic. Published statistics seem to show that the mortality rates accompanying the different operations are within a few percentage points of each other, and the average mortality the country over will probably not exceed 5 per cent. The morbidity rates vary more than the mortality rates with the different methods of operation. Again let me state, that the choice of operation should be left strictly up to the operating surgeon.

*Postoperative treatment.* After the patient has had his operation, and is home from the hospital, the general or family practitioner may be called upon to supervise his convalescence and follow up treatment, if the patient lives a good distance from the surgeon. Attention to the bladder in the form of irrigations and instillations, to clear up the infection which is practically always present, is usually ad-

visable. The administration of urinary antiseptics for a considerable period of time after surgery is also usually necessary. Good postoperative and follow up treatment after prostatic surgery is more important than it is after many other operations.

#### SUMMARY

Whereas our efforts to cure the prostatic are still beset with pitfalls, when patients in this age group can undergo major surgery with a mortality rate not over 5 per cent, and with return of reasonable urinary function, we can point with pride to the remarkable progress made in this department of surgery in the last 25 years.

#### CONCLUSIONS

1. The examination, diagnosis, and differential diagnosis of cases suspected of prostatic obstructive disease have been briefly reviewed.
2. Choice of non-operative versus operative treatment has been considered.
3. The importance of allowing the surgeon to select the operation best suited to the case has been stressed.

#### DISCUSSION

Dr. W. A. Reed (New Orleans): Dr. Hargrove's paper on prostatism was very excellent, and I enjoyed it. There is very little I wish to add, or mention, in discussing it, other than to bring up a point concerning treatment.

Dr. Hargrove deliberately did not mention treatment because, as he stated, his paper was written for the medical profession as a whole and not for the urologist. But treatment of these cases is important to all of us.

I agree with him that some patients with huge prostates do not require treatment. Occasionally we will see an individual with a large prostate, that we probably could grade as a "three or four", who has no residual urine. The reason for this is that his enlargement is produced by lateral lobe hypertrophy, as you saw in his slides, and that the median lobe is not involved, so that he does have a channel through which he can void his urine, in spite of the enlarged gland.

I agree with him, that, in many individuals who have mild symptoms of prostatism there is not only an enlargement of the prostate gland, but an associated infection as well. In a survey of such a case we frequently make the following notation: "Prostate enlarged, grade 2, plus congestion," meaning, of course, that the prostate is not only hypertrophied, but it is also enlarged due to asso-

ciated congestion. That type of prostate will often respond to local treatment.

I agree with him that you can not always predict what to expect in such a case, but many times the residual urine which may have reached three or four or five ounces will slowly diminish and eventually disappear. That patient, however, if he lives long enough, will usually require operation of one type or another, because certainly local treatment does not remove the hypertrophy.

The method of treatment of prostate hypertrophy in my opinion requires serious consideration. Many doctors feel that resection is the surgical procedure of choice. I do not always agree with them. There are many patients in whom there has been an attempt made to make the patient fit the operation, instead of selecting the operation that fits the patient. So that while we frequently do resections, we still continue to do numerous suprapubic prostatectomies and find them in many ways safer than a resection. One may resect as much as 50 or 75 grams of tissue and still leave a lot of tissue behind. There may be a few men who can remove by resection all of the prostatic tissue right down to the capsule, but there are not many of them. Certainly the average resectionist cannot do it. When too small an amount of prostate tissue is removed by resection, the balance often acts as a focus of infection as well as a continued obstruction to free urination. Furthermore it is not uncommon for a resection to bleed profusely even as long as three weeks after the operation. In cases where the prostate is unusually large and either a single or two-step suprapubic enucleation is elected as the surgical procedure of choice, the excellent end result far outweighs the disadvantage of the longer period of hospitalization that is required, over the average hospital stay that is necessary for a resection. Many patients are referred from distant towns, which makes it very difficult for them to return frequently for office treatment which is so often necessary following a resection, and almost never needed after an enucleation.

Lastly, considerable time is required to remove by resection the required amount of tissue from a large gland, which naturally results in marked trauma of the urethra, and in many instances, urethral strictures, which then require treatment indefinitely.

Dr. Robert F. Sharp (New Orleans): There are several points brought out in Dr. Hargrove's paper which I would like to further emphasize.

The first thing on which I wish to comment, is

the question of the general practitioner leaving to the urologist the type of procedure to be selected for each individual case. The closed operation, or the transurethral resection, appeals to the patient so readily that once it has been offered him, he is likely to be prejudiced against the other types of open operations, such as suprapubic prostatectomy or perineal prostatectomy. This frequently makes it difficult to get the patient to consent to the procedure that is preferable in his individual case. Every urologist naturally does not possess the same skill in doing transurethral resections and consequently a case that might be suitable for resection in the hands of one man, would not be in another. We have found, as time has gone by and we have improved our technical ability, that there are fewer and fewer cases in which we have to resort to the open operation.

The next point which I wish to make is that these patients be urged to see the urologist early in the course of their illness, instead of waiting until the case has become advanced and as Dr. Hargrove brought out, they have strained out their hemorrhoids and developed inguinal hernias. In such cases as these just mentioned, the bladder has undergone numerous changes and frequently has lost a great deal of its emptying ability and even after complete removal of the obstruction, the urinary function is not restored to normal as it would have been had the case not been neglected so long. This responsibility of getting the patient in to see the urologist early is of course, that of the family doctor. In persuading the patient to see the urologist at an early point in his prostatic illness, it will be necessary for the family doctor to alleviate his fear of this operation. Due to the reputation that the management of prostatism has had for many years, most of these old men have a real fear of having anything done to the prostate. This fear is absolutely unwarranted in modern urological treatment. Both the mortality and the morbidity in these cases is extremely low. It is surprising how well these aged patients tolerate prostatic surgery. Most of these old men were primarily endowed with a good constitution, otherwise they would never have lived to such an advanced age.

By careful management, preventing all shock, more than replacing any blood-loss, and getting them out of bed within two or three days, these people tolerate surgery as well as any other age group.

I want to compliment Dr. Hargrove on his excellent presentation of a most important subject.



## NEW ORLEANS

## Medical and Surgical Journal

*Established 1844*

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## HISTOPLASMOSIS

Recent investigations have revealed a discrepancy between the number of individuals having calcified lesions in the chest x-ray and tuberculin reaction in those individuals. In years past, when mass surveys for tuberculosis were done it was by means of a tuberculin test. In recent years, this has been supplemented by further study in the form of mass x-rays. It was found that in certain areas the number of individuals with a positive tuberculin was

not in proportion to the number of chest x-rays with calcified lesions. The area in which this was particularly observed was a more or less triangular one, in which the apex extended to the lower Mississippi Valley and the base two-thirds of the way up the Mississippi Valley nearly to the Great Lakes. In seeking an explanation for this, it was felt that some infection should be sought, which was present in the area mentioned. It was observed that the largest number of cases of acute fulminating histoplasmosis were reported from this area. The suggestion was, therefore, that this disease in a form milder than that usually recognized was responsible for these calcium deposits. A search for such cases has continued. An antigenic substance was prepared by Zarafonitis and Lindberg. This was given the name of histoplasmin and consisted of a suspension of histoplasma capsulatum grown from broth culture. This histoplasmin produced skin reactions similar in appearance to those obtained from the use of tuberculin. Skin testing has been carried out by various investigators. Palmer tested 3000 student nurses in widely separated areas. It was found that 23 per cent were positive to histoplasmin. Ten per cent had pulmonary calcification. Only one-fifth of the 300 with pulmonary calcification were positive to tuberculin; whereas two-thirds of this same 300 were sensitive to histoplasmin. It is noted, however, that there were 9 per cent who had calcifications, who reacted to neither antigen.

The states with the highest number of reactors were: Ohio, Indiana, Illinois, Missouri, Kansas, Kentucky, Tennessee, Arkansas, and Louisiana.

The significance of this reaction to histoplasmin has been questioned in various quarters. It was found by Emmons, that in guinea pigs with experimental histoplasmosis, positive reactions for histoplasma were obtained. Also, positive reactions were obtained in guinea pigs with experimental blastomycosis, coccidioidal mycosis, and haplomyosis. The same investigator tested for comparison 136 mental patients, of whom one-half had chronic atypical pul-

monary lesions of unknown etiology and the other half had no demonstrable pulmonary pathology. The results were as follow, distributed equally between the clinical groups:

Positive reactions to histoplasmin	55
Blastomycin	35
Coccidioidin	5

Studies in various fields have shown that there is a wide variation in sensitivity, depending upon location, and this is suggestive that the abundance in supply of the infectious agent is varying in the same proportion.

Up to 1945, histoplasmosis was almost a medical curiosity, in which identification was brought about entirely through laboratory means. As result of the stimulation attendant on such observations as those noted above, search has been made for non-fatal, and possibly subclinical cases of his-

toplasmosis. In line with such efforts, three nonfatal cases of histoplasmosis have been detected recently in Kansas City alone. The report from the U. S. Public Health Service states that among 72 asymptomatic cases in school children in Kansas City, a few were limited to the lymph nodes, or were of the disseminated type. Two-thirds approximately were nodular with sharply circumscribed foci.

Lesions tend to calcify slowly. Many infiltrations persist without complete calcification during a period of two years of observation. Where histoplasmin sensitivity is widespread, pulmonary infiltrations, as well as calcifications, may not be tuberculous. Accordingly, tuberculin tests and the histoplasmin test will be useful in differentiating pulmonary lesions in which the infiltration is marked and when acid fast is not found in the sputum.

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## ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

***An informed profession should be a wise one.***

### REPORT OF COMMITTEE ON RESOLUTIONS

On behalf of the House of Delegates and members of the State Society in attendance at the 1948 Annual Meeting it is desired that thanks be expressed to the following individuals and organizations for their cooperation and assistance in arranging for this meeting.

Dr. John G. Snelling, Chairman of the Committee on Arrangements, for the time and thought given to details prior to and during the meeting.

The Ouachita Parish Medical Society, host of the meeting, for wonderful hospitality and cordiality.

The Secretary-Treasurer of the State Society and personnel of his office for their capable handling of routine, as well as unforeseen matters.

Dr. Donovan C. Browne, General Chairman of the scientific program, who with the cooperation of sectional chairman, gave this feature of our meeting his wholehearted attention.

Guests on our scientific and open meeting programs who contributed a great deal in making the meeting an interesting and enlightening one.

The press and Radio Station KNOE for their generous contribution of space and time for publicity during and prior to the meeting.

The Louisiana State Board of Medical Examiners for their annual report submitted by the Secretary.

The members of the Woman's Auxiliary for their interest and cooperation.

The commercial exhibitors who, in a limited space, provided exhibits worthy of review by all members present.



Companies which continued to demonstrate their loyalty to the medical profession by placing advertisements in the program and also companies in Monroe which, for the first time, participated by advertising.

Mr. E. C. Gibson, Manager of the Frances Hotel, Mr. L. J. Hulin, Manager of the Virginia Hotel and Mr. Roger Dishongh, Manager of the Alvis Hotel, for their efforts to accommodate members and guests in attendance at this meeting and also furnishing of facilities for various sessions and social functions.

The Junior League of Monroe for assistance furnished at the registration desk.

Dr. A. V. Friedrichs, Chairman of the House of Delegates, for his capable manner in expediting business brought to the attention of the group.

To all officers and members of the Society for their attendance and manifested interest in the meeting.

#### Recommendation

1. That a copy of this report be incorporated in the minutes of this meeting and that a copy be submitted to the New Orleans Medical and Surgical Journal for publication.

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### REPORT OF COMMITTEE ON MEDICAL DEFENSE

Since the 1947 meeting of the State Society three cases have been referred to the Committee on Medical Defense. All three of these, one a case against a doctor of Shreveport, one a joint case against two doctors, one of Morgan City and the other of Houma, and a joint case against three doctors of New Orleans, were considered worthy of defense by the State Society. The material concerning these cases has been referred to the attorney employed by the Medical Defense Committee and the cases are receiving proper attention from him.

Financial reports of the Medical Defense Fund are on file in the office of the State Society and may be reviewed by any member desiring to do so.

### 1948 ANNUAL MEETING

The 1948 Annual Meeting, held in Monroe April 12-14, is considered one of the outstanding meetings of our organization. The attendance exceeded expectations, there being 347 members and 43 guests present. The scientific program was most interesting, the House of Delegates meeting efficiently and capably managed and the social features enjoyed to the fullest extent by all present.

Following is abstract of minutes of the meeting of the House of Delegates and also copy of reports of the Committees on Medical Defense and Resolutions.

#### ABSTRACTED MINUTES

#### HOUSE OF DELEGATES

##### ROLL CALL

First session: 77 delegates, 14 officers and 10 past presidents present.

Second session: 28 delegates, 13 officers and 5 past presidents present.

##### MINUTES

Minutes of 1947 meeting of House of Delegates and of Executive Committee since 1947 meeting approved.

#### SPECIAL ORDER

List of members who died since 1947 meeting read.

Approval of motion that Mr. Frank Lais, Jr., Executive Director of the Louisiana Physicians Service and Council on Medical Service and Public Relations be allowed to attend meeting of the House.

Recognition of fraternal delegates and guests: Dr. Tom B. Throckmorton, Des Moines, Iowa, Dr. O. B. Weinert, St. Louis, Missouri and Dr. Morris Fishbein, Chicago, Illinois.

#### COMMUNICATIONS

Naval Air Reserve Training Command in re need for Naval Reserve Medical Officers: Received and filed.

National Health Assembly in re refusal of invitation for Mr. Frank Lais, Jr. to attend conference May 1-4: Letter to be sent to Mr. Oscar R. Ewing advising him that hotel reservations were not requested for Mr. Lais and that this organization had expected an invitation to attend.

American Medical Association in re draft of physicians and containing opinion of the AMA in this regard with request that this organization send a similar opinion to the Senate Committee on Armed Services, to the House Committee on Armed Services and to Louisiana Senators and Congress-

men in Washington: Secretary appointed to follow out request made in this telegram.

### ACTION TAKEN

Approval of suggestion that lapel pin be awarded members who have practiced medicine fifty or more years.

Following trustees elected for a term of one year, from whom the Louisiana Physicians Service, Inc. will elect their Board of Directors: Drs. Rhett McMahon, G. C. Anderson, O. B. Owens, W. L. Bendel, H. W. Boggs, C. M. Horton, P. T. Talbot, J. P. Sanders, A. V. Friedrichs, J. W. Faulk, E. L. Zander, M. D. Hargrove, George Wright, W. P. D. Tilly, A. D. Long, and E. L. Leckert.

Following list of laymen approved, from whom Louisiana Physicians Service, Inc. will elect four members of their Board of Directors: Don Ewing, Pat Turner, H. Barrett, all of Shreveport; T. B. Bennett and S. G. Ray, Baton Rouge; H. D. Murchison, Alexandria; Frank Lais, Jr., Ed. Carriere, Ellis Hennican, Edward Groner, Ralph B. Reese and John LaNasa, all of New Orleans.

House of Delegates went on record as approving proposed action of Texas delegation to AMA in re efforts to have more equal geographic distribution of representation on Board of Trustees of AMA.

Approval of continuation of Annual Secretaries Conference similar to meeting held this year.

### MATTERS DISCUSSED—NO ACTION TAKEN

Editorial in Journal of the AMA in re rebates, kickbacks, commissions and medical ethics: No action taken, pending action of the AMA and government.

Legislative bills.

Resolution concerning activity of National Physicians Committee.

Leprosy problem.

### RECOMMENDATION OF THE EXECUTIVE COMMITTEE

That lay members be added to Board of Directors of Louisiana Physicians Service, Inc.: Approved.

### REPORTS OF OFFICERS AND COMMITTEES CONTAINING NO RECOMMENDATIONS

Following reports received and filed: Secretary-Treasurer, Chairman of Council; Councilors of First, Second, Third, Fourth, Fifth, Sixth, Seventh and Eighth Districts; Committees—Advisory to Woman's Auxiliary, Aid to Indigent Members, Budget and Finance, Cancer, Council on Medical, Dental and Pharmaceutical Services, History of L. S. M. S., Industrial Health, Journal, Louisiana Physicians Service, Inc., Medical Defense, Medical Education, Medical Testimony, Mental Health, National Emergency Medical Service, Nutrition, Pub-

lic Policy and Legislation, Rural Medical Service, Scientific Work, Study Rearrangement of Annual Meeting Programs, and Venereal Disease Control.

### REPORTS OF OFFICERS AND COMMITTEES CONTAINING RECOMMENDATIONS

President:

1. That the House of Delegates approve in principle plan for additional financial expenditure for activity of Council on Medical Service and Public Relations, for guidance of the Budget and Finance Committee—Approved. 2. Coordination of activity of Council on Medical Service and Public Relations and Committee on Rural Medical Service—Approved. 3. Employment of secretary to work with Council on Medical Service and Public Relations, Committee on Rural Medical Service and Secretary-Treasurer; preferably a Doctor of Medicine—In view of action on other recommendations, it is not felt that at the present time employment of an additional assistant secretary is necessary or desirable. 4. Board of Directors of Louisiana Physicians Service, Inc. be increased to 15—No action taken in view of previous action taken in regard to addition of lay members of Board. 5. Board of Directors of Louisiana Physicians Service, Inc. may contain lay members, not to exceed four—Approved. 6. Louisiana State Medical Society select, annually, 12 laymen from whom Louisiana Physicians Service, Inc. must choose lay members of the Board of Directors of Louisiana Physicians Service—Approved. 7. That the House of Delegates consider granting an adequate increase in salary to Dr. P. T. Talbot, Secretary-Treasurer—Approved with recommendation that this salary be increased to \$7500.00 per year; also that the salary of the Assistant Secretary-Treasurer be increased to \$3600.00 per year.

Committee on Congressional Matters: 1. That the House of Delegates reaffirm opposition to Senate Bill 1290 and House Bill 1980 and that Louisiana Congressmen and Senators in Washington be notified accordingly—Approved.

Committee on Corresponding Library for Members of State Society: 1. Discharge of the committee is requested and recommended—Approved.

Committee on Hospitals: 1. That the House of Delegates and officers of the State Society consider the report and activities of the Committee on Hospital Licensure of which Dr. Paul Kurzweg is Chairman—Upon recommendation of Chairman of Committee on Licensure Law for Hospitals, report referred to Committee on Public Policy and Legislation. 2. That all hospitals in the state equip the ambulances serving their institutions in accordance with the state law—Approved. 3. That all hospitals in the state have proper equipment for emergency care of the injured—Approved.

Committee on Juvenile Delinquency: 1. That a Committee on Juvenile Delinquency be continued



as a special committee of the Louisiana State Medical Society—Approved.

Committee on Licensure Law for Hospitals: 1. That the report of the special committee on hospital licensure (referred to in the report of the Committee on Hospitals) be referred to the Committee on Public Policy and Legislation for review—Approved.

Committee on Maternal Welfare: 1. That the Louisiana State Medical Society endorse such a study (complete survey of maternal and fetal deaths) as a very worthy venture for the public, the doctors and the medical society—Approved with the further recommendation that the Secretary be instructed to so advise the Director of the State Department of Health, Dr. W. L. Treuting, who has stated he will cooperate in handling of the project if approved by the State Society. 2. That an appropriation of \$2,000.00 be approved for the survey this year—Not approved.

Committee on Resolutions: 1. That a copy of this report be incorporated in the minutes of this meeting and that a copy be submitted to the New Orleans Medical and Surgical Journal for publication—Approved.

Committee on Tuberculosis: 1. That the proposed Five Year Plan be re-submitted to the Committee on Tuberculosis and that said Committee be charged to study the plan fully—Approved.

#### REPORT OF COUNCIL ON MEDICAL SERVICE AND PUBLIC RELATIONS

1. That an appropriate resolution be directed to the cooperating radio stations acknowledging their participation by their contribution of radio time for use by the Council on Medical Service and Public Relations in the presentation of its health program—Approved. 2. That an appropriate resolution be directed to the newspapers throughout Louisiana acknowledging the assistance given in the presentation of news to the general public in behalf of the medical profession—Approved. 3. That the House of Delegates approve an adequate budget for the continued operation and expansion of the services offered by the Council on Medical Service and Public Relations—Appropriation of \$10,000.00 approved. 4. Request approval of American Association of Blood Banks—Motion made and carried that the State Society support this Association. 5. Endorsement of Health, Physical and Safety Education Program—Approved.

#### REPORT OF LOUISIANA PHYSICIANS SERVICE, INC.

1. That four lay members be added to Board of Directors of Louisiana Physicians Service—Approved.

#### REPORT OF LOUISIANA STATE BOARD OF MEDICAL EXAMINERS

Report accepted and following members recommended to Governor for appointment to fill vacancy in re Dr. Rhett McMahon: Drs. Rhett McMahon, Charles McVea and W. J. Norfleet.

#### ELECTION OF OFFICERS, COMMITTEES AND DELEGATE AND ALTERNATE TO AMA

President-elect—Dr. Edwin H. Lawson, New Orleans.

First Vice-President—Dr. John G. Snelling, Monroe.

Second Vice-President—Dr. Ashton Thomas, New Orleans.

Third Vice-President—Dr. T. A. Richardson, Minden.

Chairman, House of Delegates—Dr. A. V. Friedrichs, New Orleans.

Vice-Chairman, House of Delegates—Dr. J. P. Sanders, Shreveport.

Councilor, First District—Dr. Edwin L. Zander, New Orleans.

Councilor, Second District—Dr. Joseph Kopfler, Kenner.

Councilor, Fourth District—Dr. Paul D. Abramson, Shreveport.

Councilor, Fifth District—Dr. George Wright, Monroe.

Committee on Journal: Dr. C. M. Horton, Franklin; 3 year term.

Committee on Medical Defense: Dr. C. B. Erickson, Shreveport, Chairman; 3 year term. Dr. Sam Hobson, New Orleans; 1 year term.

Committee on Public Policy and Legislation: Dr. Roy B. Harrison, Chairman; Dr. C. G. Cole, Dr. P. T. Talbot, all of New Orleans; Dr. King Rand, Alexandria; Dr. M. D. Hargrove; all for 1 year term.

Committee on Scientific Work: Dr. P. T. Talbot, Chairman; Dr. W. H. Gillentine; both of New Orleans; Dr. J. E. Knighton, Jr., Shreveport; all for 1 year term.

Delegate to AMA 1949 and 1950—Dr. Val H. Fuchs, New Orleans.

Alternate to Delegate to AMA 1949 and 1950—Dr. George Hauser, New Orleans.

#### PLACE OF 1949 MEETING

Invitation to hold the 1949 Annual Meeting in New Orleans was accepted.

## LOUISIANA STATE MEDICAL SOCIETY NEWS

## CALENDAR

## PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

## SECOND DISTRICT MEDICAL SOCIETY

The monthly dinner meeting of the Second District Medical Society met on March 25 at 4800 Airline Highway. A symposium on fractures was presented. Dr. Morgan Lyons described types of fractures; Dr. Dan Baker discussed etiology and treatment of fractures; Dr. Gilbert Anderson, president of the State Society, discussed neurological signs and symptoms of fractures; Dr. Lyon K. Loomis discussed orthopedic procedures; Dr. Robert Sharp discussed the urologic angles of fractures. Members present were: Drs. Kohlman Gauthier, John W. Atkinson, Joel B. Gray, Robert Sharp, William Clark, Lyon K. Loomis, Martial B. Casteix, Adrian B. Cairns, and John Earl Clayton. Guests in attendance were Drs. Gilbert Anderson, Morgan Lyons, Dan Baker, Everett L. Drewes and J. J. Bosch (DDS.)

At the April dinner meeting on April 15, the members and guests were given a vivid, accurate and comprehensive review of the Louisiana State Medical Society Meeting at Monroe April 12-14. President Robert Sharp formally introduced the new Councilor of the Second District, Dr. Joseph Kopfler of Kenner. Dr. Kopfler is one of the charter-founder members of the Second District Medical Society and is the oldest, in point of service, member of the organization. The Secretary, who was the official delegate, gave a summary of the events which occurred in the House of Delegates. Members present were Drs. William B. Clark, Robert F. Sharp, Lyon K. Loomis, Floyd Hindelang, Earl Kent, John W. Atkinson, John Earl Clayton, Joseph S. Kopfler, Joel B. Gray, Martial B. Casteix and Philip P. LaBruyere. Guests were Drs. Vincent D'Ingianni, J. D. Mateau (DDS) and W. Jay Elmer (DDS).

The next regular monthly dinner meeting of the Society will be held at Wigwam Restaurant, 4800 Airline Highway, Thursday evening at 8:00 p. m. on May 20. Dr. A. V. Friedrichs, Chairman of Council on Medical Service and Public Relations of the Louisiana State Medical Society, will demonstrate charts and exhibits shown to the House of Delegates at the State Society meeting

in Monroe. Reservations for dinner (\$3.00) may be obtained through the Secretary, Dr. Joel B. Gray, 476 Metairie Road, New Orleans 20.

## POSTGRADUATE COURSE IN PEDIATRICS

Under the sponsorship of Louisiana State University School of Medicine and Louisiana State Department of Health a postgraduate course in pediatrics was conducted for the period April 5-9 inclusive. Some thirty-five practicing physicians from the less densely populated areas of the state were in attendance. The course was at Louisiana State University School of Medicine and in the wards of Charity Hospital and covered many of the more important phases of pediatrics.

Speakers from outside the state included Dr. Harold E. Harrison, pediatrician-in-chief, Baltimore City Hospital, and associate professor of pediatrics of the John Hopkins University and Dr. Horace L. Hodes, medical director Sydenham Hospital and associate professor of pediatrics of the Johns Hopkins University. Dr. Vernon W. Lipard, dean of L. S. U. School of Medicine, Dr. Myron E. Wegman, professor of pediatrics and other members of the faculty of medicine also took part.

This course is part of the continuation program for the practicing physicians of the state which L. S. U. and the Louisiana State Department of Health are developing both at the university and throughout the state.

## NEWS ITEMS

Doctors C. Merrill Whorton and Frank C. Womack will join the faculty of the School of Medicine, Louisiana State University, as assistant professors of pathology on July 1, 1948. Dr. Whorton is at present associated with the Mallory Institute of Pathology at Boston City Hospital and is now on the staff of Tufts Medical College. He graduated at Vanderbilt University in 1941 and during the war was a member of the malaria research unit at the University of Chicago. Dr. Womack is at present an instructor in pathology at the Vanderbilt University School of Medicine.



He also received the M. D. degree at Vanderbilt in 1941 and served in the Navy during the war.

A grant of \$15,364 has been received from the War Department for continuation of studies on bacitracin in the Department of Surgery. The investigation was inaugurated on July 1, 1947 on a previous grant of \$15,222 from the same source.

The National Cancer Institute, U. S. Public Health Service, has awarded to the School of Medicine, Louisiana State University, a grant of \$19,941 effective July 1, 1948 for development of the teaching and research programs in cancer. Dr. Walter J. Burdette, assistant professor of surgery, has been designated coordinator of the cancer program.

#### CANADIAN ROCKY MOUNTAIN VACATION

The Oklahoma State Medical Association announces through Dick Graham, Executive Secretary, that they will sponsor for the third time a post convention tour in conjunction with the AMA convention which is to be held this year at Chicago June 19-25. They wish to extend a special invitation to the physicians and wives of Louisiana to join them on their trip to the Canadian Rockies.

This 13 day tour is all-expense and starts from Chicago on Friday, June 25 at 1:15 p. m., at the close of the AMA Convention. They will visit Jasper National Park, Columbia Icefield, Lake Louise, Banff, as well as spending one day at the Calgary Stampede before returning back to Chicago on July 7. The trip includes the choice of menu, finest of hotels with de luxe Pullman accommodations as well as complete sightseeing program. All transfers and baggage handling are also included. The tour will be under the personal direction of Mr. Harry E. Kornbaum who has conducted the two previous Oklahoma Medical Association Tours, last year Quebec and the previous year to San Francisco and the Pacific Northwest.

This tour will be a special train and limited to 130 reservations. Pullman accommodations will be assigned in order of reservations received. For those who are interested, write direct to Mr. Dick Graham, executive Secretary, Oklahoma City, Oklahoma. A complete day by day itinerary with prices will be forwarded.

#### SOUTHERN PEDIATRIC SEMINAR

The Twenty-eighth Annual Session of the Southern Pediatric Seminar is to be held at Saluda, North Carolina, July 5-July 17. This pediatric organization was recently incorporated as a nonprofit endeavor, dedicated to the cause of pediatrics in the South. Its efforts in the past have been directed toward betterment of pediatrics in its many phases, and the presentation of a well-rounded, short course in which Southern pediatricians give papers and conduct discussions.

There are some 72 sessions spread over a period of two weeks. The time of the visiting pediatri-

cian appears to be occupied in full from 9:00 in the morning until 4:30 in the afternoon. There are six night sessions, some of which are devoted to the problems of pediatrics, and some to the lighter phases of the pediatricians' existence.

The program appears to be a very inviting one. The prospect is that the session will be enjoyed profitably and pleasurably during this July meeting as they have been in the past.

#### MEDICAL ALUMNI DINNER

University of Pennsylvania Medical Alumni will hold a dinner at the Convention of the American Medical Association in Chicago, Wednesday, June 23 at the Lake Shore Club, 850 Lake Shore Drive. On arrival in Chicago, alumni should contact Miss Frances R. Houston, Executive Secretary of the Medical Alumni Society, at the University of Pennsylvania registration booth.

#### AMERICAN UROLOGICAL ASSOCIATION

The Southeastern Section of the American Urological Association announces receipt of a \$1000 donation from Mr. and Mrs. William R. McEwen, Ft. Lauderdale, Florida. The Fund is to be used to stimulate research on the problem of "Urinary Bladder Dysfunction." An award of \$250 will be made for the best essay presented before the annual meeting of the Southeastern Section. Competition is open to men who have graduated from medical school within the past ten years. Further information may be obtained by writing to Dr. Russell B. Carson, 408 Sweet Building, Ft. Lauderdale, Florida, Secretary-Treasurer of the Southeastern Section of the A.U.A.

#### AMERICAN COLLEGE OF SURGEONS APPROVES USE OF NURSE ANESTHETISTS

The Board of Regents of the American College of Surgeons, at a meeting on February 22, adopted the following resolution commending the services of nurses who have had special training in the administration of anesthesia and recommending the continuance of training courses in this field for nurses. "The American College of Surgeons regards with deep concern the actions of some physician anesthesiologists in giving the impression to the laity in the public press that it is unsafe for experienced nurse anesthetists to conduct surgical anesthesia. While it supports the increasing tendency of having physician anesthesiologists in charge of surgical anesthesia, it deplores at this time any propaganda for the elimination of the trained nurse anesthetist. On the contrary, the American College of Surgeons is of the opinion that, in view of the inadequacy in number of the physician anesthesiologists and in view of the splendid record of achievement of

the nurse anesthetists, institutions engaged in the training of nurses for this purpose should be encouraged to continue their programs."

#### POST GRADUATE COURSES

The Chicago Medical Society is offering physicians of the country two postgraduate courses in September. A course in hematology and neurology will be given September 13-18 and another in cardiovascular and respiratory diseases will be given September 20-25.

The sessions will be held in Thorne Hall on Northwestern University Medical School campus.

An outstanding group of teachers from all sections of the United States will make up the faculty.

Information may be secured by writing the Chairman, Committee on Postgraduate Medical Education, Chicago Medical Society, 30 North Michigan Avenue, Chicago 2, Illinois.

#### SAN ANTONIO ASSEMBLY

The International Post-Graduate Medical Assembly of Southwest Texas will be held in San Antonio, Texas, January 25-26-27, 1949. Dr. Boen Swinny, San Antonio, Texas, President; Dr. John J. Hinchey, San Antonio, Texas, Secretary.

#### WOMAN'S AUXILIARY

In the March 26 issue of the Shreveport Journal articles and pictures on "The Preservation of Medical Cultural Items" were given noticeable space. This work was most outstanding and Caddo Parish is to be complimented on such a outstanding accomplishment. Caddo Parish has given this interesting project the enthusiasm it deserves and their work in turn gives the general public an awareness of what our Auxiliaries can accomplish.

The Woman's Auxiliary to the American Medical Association extends a most cordial invitation to all women who are Auxiliary members or guests of physicians attending the convention of the American Medical Association to participate in all social functions and attend the general sessions. Whether Auxiliary members or not, the wives of doctors will be most welcome.

The American Medical Association's twenty-fifth Annual Meeting, or Convention, is to be held in Chicago, June 21-25. Headquarters will be at the Hotel LaSalle.

I wish to thank the members of the Advisory Committee of the Louisiana State Medical Society, the Auxiliaries and the New Orleans Medical and Surgical Journal for their splendid co-operation during my year as Press & Publicity Chairman and extend my best wishes and support to your new Press & Publicity Chairman.

Mrs. Charles E. Allen, Jr.,  
Press & Publicity Chairman.

## BOOK REVIEWS

#### *Curare. Its History, Nature, and Clinical Uses*

By A. R. McIntyre, M. D., Ph. D. Chicago, The University of Chicago Press, Publisher, 1947. Pp. 240. Price, \$5.00.

This publication is timely due to the current interest in the clinical use of curare. The author is well qualified to review this subject. Dr. McIntyre, Professor of Pharmacology in The College of Medicine, University of Nebraska, has been actively engaged in a laboratory study of the action of curare for several years. He has also been in close touch with clinical developments in this field as a result of his own observations and through those of his associate Dr. A. E. Bennett who has had extensive experience with the use of curare in patients.

Particularly interesting to the reviewer are the chapters concerned with the historical and geo-

graphical aspects of the subject, including numerous verbatim accounts of the early explorers of the Amazon, Orinoco and Essequibo river basins. A review of the sources of curare has been difficult due to the indefinite botanical information supplied by early investigators but the literature of the past twenty years has done much to bring order out of chaos. Although a number of alkaloids have been isolated from various preparations of curare, information relating the principles to botanical sources is largely speculative. A notable exception in this regard is that of d-tubocurarine, the important constituent of Intocostrin, the source of this alkaloid being established as *Chondrodendron tomentosum*. Various species of *Chondrodendron* and of *Strychnos* are the principle if not the only sources of the curare alkaloids.

In the chapters dealing with the action of curare particular attention is given to the well known



peripheral effect on skeletal muscle. Experiments with curare in the 19th century were intimately associated with the elucidation of nerve-muscle physiology and this is true to a considerable extent even to the present time. It would be a difficult task to confine an adequate review of the extensive literature within reasonable limits, however a possible criticism is that the chapters on this subject might have been amplified to some extent. For a reader not already conversant with the literature of this field, it is difficult to appreciate the significance of the discussion in many instances. The author believes that the action of curare and of other drugs affecting its action are most readily explainable by acceptance of the theory of chemical mediation of the nerve impulse to skeletal muscle.

In addition to the discussion of the typical action of curare on skeletal muscle, other less known actions are reviewed including those on the circulation, respiration, viscera and on miscellaneous functions and structures. Of interest, particularly in relation to its use in general anesthesia, is evidence for a depressant action on the central nervous system. In a consideration of the clinical uses of curare attention is given to early attempts to apply its action in tetanus and in certain other conditions. The availability of a standardized preparation in recent times has given impetus to a variety of applications, particularly in shock therapy and in general anesthesia. The author realizes that the present recommendations of its use as a therapeutic agent may have to be modified and takes a conservative attitude regarding its true or ultimate value, pointing out also that much is still to be learned regarding its effects on neuromuscular metabolism.

Interest is added in that the book is not only a review of the literature but is interspersed with references to the author's personal researches and opinions on various phases of the subject. An extensive bibliography accompanies each chapter and a subject and author index is appended.

RALPH G. SMITH, M. D.

*Synopsis Of Obstetrics:* By J. C. Litzenberg, B. Sc., M. D., F. A. C. S., St. Louis, C. V. Mosby Company, 1947. 3rd ed. Pp. 416. Price, \$5.50.

In the third edition of this book, which contains 157 illustrations, the author has added not only

the usual corrections and revisions of a new edition, but has completely rewritten the following subjects in this synopsis of obstetrics:

1. The diagnosis of pregnancy, with especial reference to trustworthy laboratory tests of pregnancy.
2. Relief of pain in labor.
3. Diabetes in pregnancy.
4. Puerperal infections and skin treatment with sulfonamides and penicillin.
5. The relation of the Rh factor to pregnancy.

In reading the entire synopsis one notes that a few well established facts were not considered by the author:

1. The effect on the fetus of certain infectious diseases in the mother, particularly German measles.
2. The importance of the midplane contraction.
3. The use of podophyllin in condyloma acuminata.
4. Amniotic fluid as a cause of pulmonary embolism and sudden death of the mother.
5. The use of the sympathetic block in the treatment of thrombophlebitis of the lower extremity.
6. The use of antibiotics and chemotherapy prophylactically in prolonged labor.

Two recommendations cannot be accepted:

- a) The emphasis of median episiotomy over the safer medio-lateral type and
- b) The induction of labor in eclampsia, following the control of convulsions by the use of bougies and bags.

Otherwise this continues to be an excellent, brief but reasonably adequate discussion and evaluation of obstetrics.

CALVIN M. JOHNSON, M. D.

#### ALLERGY IN THEORY AND PRACTICE

*Allergy in Theory and Practice:* Robert A. Cooke, M. D., Sc. D., F. A. C. P., W. B. Saunders Company, Philadelphia, 1947. Pp. 572. Price, \$8.00.

This book is an excellent condensation of the present day concepts of clinical allergy. It clearly represents the opinions of Dr. Cooke, and to a great extent the ideas of the Eastern group of allergists. Dr. Cooke was one of the pioneers in clinical allergy, and he has therefore a first hand knowledge of the development of this specialty.

He, himself, has been a most important contributor.

He clearly recognizes the importance of infection in allergic states. His chapters on the respiratory manifestations of allergy emphasize the importance of this factor, and provide the clinical allergist with a great deal of sound information. He is attending Physician and Director of the Department of Allergy at the Roosevelt Hospital in New York, and many studies on the association of sinus infection with these allergic states have been made in this institution.

Because of his comprehensive knowledge, Dr. Cooke has been able to assemble and clarify our ideas on various topics. He suggests some new clinical classifications, which are improvements on the older ones. For instance, he divides the two main varieties of allergic dermatitis into the extrinsic (contact) and intrinsic (neurodermatitis) types. He feels that the two conditions are closely related, and therefore an antigen may at times produce dermatitis by ingestion or by external contact. There are many fine illustrations in the book.

Various eminent contributors aided him, and wrote several of the chapters. However, there is one criticism which should be made. A prominent local ophthalmologist made several criticisms of the chapter on allergy of the eye. These remarks would not have been justified if the material had been assembled with the assistance of an ophthalmologist. However, it is most likely that an ophthalmologist did read the chapter, and that these local criticisms may not represent anything more than a difference of opinion. No two medical men think exactly alike on any topic.

All in all I consider this book to be a very valuable contribution, and should particularly be read by otorhinolaryngologists, dermatologists, and pediatricians. In several medical specialties, the importance of the allergy factor has too often been overlooked, disregarded, or inadequately handled. The book provides an effective way for medical men to gain accurate knowledge of the interrelationship of allergy to various fields of medicine, and gives them an idea of the complexity and detail connected with the specialty of allergy. Allergy is now a definite field of medicine and can no longer be ignored.

HENRY D. OGDEN, M. D.

*Four Hundred Years of a Doctor's Life:* By George and Beate Caspari-Rosen, M. D. New York, Schuman, 1947. Pp. 429. Price, \$5.00.

A most interesting and unique book. The years of a doctor's life from the cradle to the grave are dealt with in the form of excerpts from the biographies and autobiographies of the great and near great in medicine. In numbers, he quotes from the lives of over eighty doctors. In time he traverses four centuries. The choice of a vocation and an avocation are charmingly related and selections from poems and letters add considerably to the book. They depict doctors turned literati, and politicians and other professionals turned medicos for their happiness and comfort.

One may spend hours of real pleasant reading. If one looks for the ingredients that make for success, he finds in all the same components, but in each the proportions vary and that is the elusiveness in the search for the formula of triumph. One gains the impression as he reads this volume that the important thing is not that humans have so many weaknesses, but that despite these many frailties they are able to rise to such great heights and overcome wellnigh impossible obstacles in their paths.

The format of the book is good. There is a good bibliography which should prove of interest to anyone interested in reading still farther into the lives of their medical ancestors of every roll and clime, and of all positions in society.

I. L. ROBBINS, M. D.

*Textbook of General Surgery:* By Warren H. Cole M. D., F. A. C. S. and Robert Elman, M. D., F. A. C. S. Appleton-Century Company, New York, 5th Ed., 1948. Pp. 1160. Price, \$11.00.

The 5th edition of Cole and Elman's Textbook of General Surgery brings up to date the advances in surgery which have developed since the publication of the previous edition. This includes antibiotic therapy, surgery of congenital vascular anomalies, surgery of the sympathetic nervous system and recent advances in thoracic surgery.

The basic principles and practical considerations of the surgical diseases are clearly and briefly reviewed. Controversial material and lengthy discussions are omitted, while diagnostic and therapeutic methods most readily adaptable for use in general practice have been stressed by



the authors. An appropriate bibliography is included after each chapter for those who wish detailed reading.

ERNEST DEBAKEY, M. D.

*Pharmacology, Therapeutics and Prescription Writing*: By Walter Arthur Bastedo, Ph. G., Ph. M. (Hon.), M. D., Sc. D. (Hon.), F. A. C. P. 5th Ed. Philadelphia, W. B. Saunders Company, 1947. Pp. 840. Price, \$8.50.

The present edition of this well known textbook is an extensive revision of that which appeared in 1937. The rapid advances in pharmacology and drug therapy which have been made since that time have necessitated also the addition of several new sections. In the latter connection consideration is given to therapy with amino acids, the use of blood, blood fractions and blood substitutes and to the pathologic physiology of shock and its management. The newer coagulant preparations such as thrombin, fibrin foam, gelatin sponge, vitamin K and the anticoagulants heparin and dicumarol receive special attention. Naturally the sulfonamides and antibiotics also receive adequate coverage. In a further list of newer drugs there may also be included folic acid, rutin, propyl thiouracil and BAL. The section of digitalis shows considerable revision in keeping with the increasing importance of pure glycosidal preparations in present day therapy. Likewise the section on the treatment of syphilis has been rewritten to include the use of the more recent preparations of arsenic and bismuth and modern theories of action of the former. Of course penicillin is also considered in this connection. The above citations are by no means a comprehensive list of the revisions but merely illustrate their nature. In addition to therapeutic agents the actions of some of the more important poisons such as carbon monoxide, cyanides and lead are discussed. The section on tobacco is more extensive than those in most textbooks of pharmacology. As in previous editions some twenty pages are allotted to prescription writing. One deficiency from the standpoint of the modern student is the dearth of structural formulae. In view of the present interest in the relationship of chemical structure to pharmacologic action such information would be appreciated. A second shortcoming is the lack of either sectional or general bibliographies. Although in the text the name of the author with date is commonly mentioned this practice does not make the reference as easily available.

The general approach to the subject of pharmacology has not been modified from previous editions. As stated by the author in the preface \* \* \* "our guide throughout has been the need of the physician who employs drugs in the treat-

ment of sick patients." In other words the book is written essentially with a therapeutic approach and should be of interest and value to the practicing physician.

RALPH G. SMITH, M. D.

*A Manual of Pharmacology and Its Applications to Therapeutics and Toxicology*: By Torald Sollmann, M. D. 7th Ed. Philadelphia, W. B. Saunders Company, 1948. Pp. 1132. Price, \$11.50.

Those who are familiar with previous editions of this text will be immediately impressed by the new format of two columns on a somewhat larger page. In other respects, such as the arrangement of subject matter and the general nature of its presentation there is little change. In each section a digest of the subject under consideration appears in regular type. This is followed, in small type, by more detailed information and citations from the literature. The subject of pharmacology is covered systematically with stress on those drugs used in modern therapy. As has been the case with each revision there is some abridgement of information on drugs falling gradually into disuse to make way for newer medicaments. This however, is particularly true in this edition, appearing after the extensive developments of the war years. New emphasis is placed on chemotherapy with the inclusion of the antibiotic agents and of advances made in our knowledge of the sulfonamides, antimalarial agents and those antimonials which are of value in the treatment of certain tropical diseases. The antihistaminic and antithyroid drugs, folic acid, purified preparations of curare, dicumarol and the nitrogen mustards receive attention. More space is given to heparin, vitamin K and purified glycosidal preparations of digitalis than previously, in keeping with increasing experience with these compounds. Further, the text is not restricted to therapeutic agents but contains information on the more common poisons, and the recently developed insecticides, rodenticides and weed killers. From the standpoint of the variety of subject matter "Sollmann" is more comprehensive than most textbooks of pharmacology and a student of this subject may find much detailed information here not readily available elsewhere. The usual extensive bibliography has been revised and restricted to papers which have appeared within the past twenty years. "Sollmann" is not as readable as many works of fiction but it is recommended as an excellent up-to-date reference book on pharmacology.

RALPH G. SMITH, M. D.

#### PUBLICATIONS RECEIVED

Butterworth & Co. (Publishers), Ltd., London, England and C. V. Mosby Company, St. Louis:

British Surgical Practice (8 Volumes, Volume 2), edited by Sir Ernest Rock Carling, F. R. C. S., F. R. C. P. and J. Paterson Ross, M. S., F. R. C. S.

Grune & Stratton, New York: Atlas of Plastic Surgery, by Morton I. Berson, M. D.; Biology of Disease, by Eli Moschcowitz, M. D.

Institut Pasteur D'Algérie, Algiers: Histoire d'un Marais Algérien, by Edmond Sergent and Etienne Sergent.

Johns Hopkins Press, Baltimore: Scientists Starred 1903-1943, by Stephen Sargent Visher.

Lea & Febiger, Philadelphia: Clinical Toxicology (2nd edition), by Clinton H. Thienes, M. D., Ph. D. and Thomas J. Haley, Ph. D.

McGraw-Hill Book Company, Inc., New York:

You and Your Doctor, by Benjamin F. Miller, M. D.

C. V. Mosby Company, St. Louis: Physiology of Exercise, by Laurence E. Morehouse, Ph. D. and Augustus T. Miller, Jr., Ph. D.

Oxford University Press, New York: Headache, by Harold G. Wolff, M. D.

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Washington Institute of Medicine, Washington, D. C.: The Battle of the Conscience, by Edmund Bergler, M. D.



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### CLINICAL OBSERVATIONS ON THE TREATMENT OF THE ALCOHOLIC\*

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This report is based on the study and treatment of 2275 sanitarium cases of alcoholism, the majority of which were observed and studied for at least four weeks. It expresses some of the observations that I have made in the management, study and treatment of the alcoholic patient.

The alcoholic suits admirably the caption, "Sick in body and sick in mind." His case is primarily one for the psychiatrist, as alcoholism has its basic starting point in the psychic sphere. Contributing causes may be timidity, bashfulness, feelings of inadequacy or inferiority, or deeper personality maladjustments.

It is at this initial stage that psychiatrists prefer to come in contact with the case. Psychiatric consultations and guidance for these patients would prevent the progress of emotional problems, and, with proper insight and confidence restored, there would not be the resultant tensions and somatic symptoms that so often lead to a flight into alcoholism as a temporary or permanent escape mechanism.

The younger an addict started drinking the harder will be the problem of cure, possibly because of alcohol's effect on immature emotions. I have in mind those patients who started drinking during their

early high school days. A history of inebriety at the age of fourteen, fifteen and sixteen is not an infrequent occurrence.

The development of the alcoholic is, as a rule, not rapid until a certain point is reached. Alcoholism then develops with alarming rapidity. In my observation, this point is reached when the narcotic effect of the alcohol is sought. The victim then drinks to blot out, temporarily at least, all conscious memories. Frequently, under the effects of the drug, as a result of continued drinking, the waking and passing out either ends disastrously or toxic symptoms develop, such as hallucinosis, delirium tremens, partial starvation, and acute avitaminosis.

Psychiatry is the door to the hidden forces that cause the patient to become an alcoholic addict. It is my conclusion that each alcoholic patient can give the psychiatrist all the letters of the alphabet necessary to spell success in his case. There may be exceptions, but in my clinical experience these are rare. I do not mean to imply that these cases are as simple as A.B.C., but I do believe that, during the course of several weeks to two months, the psychiatrist will find the key to the case, provided the alcoholic patient is willing to cooperate and really wants the help the psychiatrist can give him. Many times I have seen a patient who would not frankly discuss his problems—even deny things I knew positively were true—and later take the attitude that he had fooled the physician. This non-cooperation on the part of the patient, even though cooperating in all other re-

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spects, cannot result in anything except failure of the patient to make an adjustment. Every psychiatrist can help every alcoholic if that alcoholic really wants help.

We, as psychiatrists, can understand these mental mechanisms of non-cooperation, but at times it is extremely difficult to get the patient to give his full response. It requires tact, diplomacy, and training, and sometimes one wonders, "Who the devil wants to be a diplomat!" The non-cooperative type will often respond to psychiatric studies after two or three weeks, whereas psychiatrically speaking prior to that time they were "untouchables." These are usually cases of constitutional inferiorities with emotional immaturity, psychoneurosis with inferiority complexes and over-compensations, and, last but not least, the schizoid personalities.

At this point we should differentiate between emotional immaturity and emotional instability resulting from the alcoholic spree or debauch. The former has never grown up emotionally and the latter is emotionally unstable as a result of an overdose of alcohol and side reactions resulting therefrom. The emotionally immature patient will often respond and cooperate if the daily visit is made for some time on a neutral ground. This type is suspicious and often thinks the psychiatrist is trying to prove that something is mentally wrong. The patient, however, will often become friendly with the physician in a few days, and with tact the psychiatric aspects of the case can be obtained; the same patient, however, had he known the physician was a psychiatrist, would not have opened up. I have had this experience several times and have been told by some of the cases that I should study psychiatry. The point is that many alcoholics are "gun shy" of psychiatrists per se but will often cooperate fully with the physician-psychiatrist.

On the other hand, there is the alcoholic who demands a psychiatrist at once and expects the psychiatrist to convince him that he is not an alcoholic and point out a clear course by which he can return to drinking socially without becoming intoxicated. Such

a course does not exist, because the alcoholic cannot remain well except by total abstinence forever, and he must never revert to social drinking.

I have seen such patients come in and profess most sincerely and earnestly that they want to get well at any cost or sacrifice. This is especially true when they are accompanied by relatives or close friends. Statements of this kind made when the patient is on the verge of cracking up, or just getting over a binge during which he causes a great deal of worry and anxiety, should not be taken too seriously, as frequently this is an effort to have the parents and friends feel sorry for him as a result of his predicament. The statements and promises made at the end of several weeks when he is returning to a normal basis are more dependable. The shame, remorse and regret manifested on admission often disappear in two or three days as the patient feels better; then we see the individual picturing his episode in a comical way, with himself as the chief comedian or hero, as the case may be. Very seldom is the sordid side ever told; incidents may be admitted, however, if the information is from some other source than the patient, but never elaborated on.

The alcoholic or the ex-alcoholic is always hoping that the time will come when he can resume drinking alcoholic beverages socially. This is a fervent hope and wish of these individuals and *this is the most frequent cause of relapse*. The false belief that some day they will again try to prove that they can control their drinking is in the mind of the majority of alcoholics. Sooner or later they will put the theory to a test and—bingo! It is certainly bad personal psychology for the patient to carry this thought in mind. It acts as a constant suggestion. On the other hand if he accepts the law that, under all circumstances, he can never drink, then the mental hazard is eliminated.

Beware the alcoholic patient who gets well in five or six days, goes around telling everyone how wonderful he feels, what a great treatment he received, that the world



is rosy in every respect, and there will be no more drinks for him. He is riding on a wave of euphoric purity based on emotionalism and not on stability of the central nervous system. He'll be drunk again in six weeks or sooner.

Many alcoholics are proud of the fact that they are alcoholics and brag about the many treatments they have taken and the many psychiatrists they have seen and they end with the lament that no one ever cured them. They often use the fact that they were treated before as proof that they are incurable. Some alcoholics want to be considered incurable and above all want their family to consider them so, in order that they may continue their indulgence without interruption or interference. It matters not that they attempt to drive while intoxicated and endanger the lives of others.

All sanitariums have a "repeater" patient who is always telling the new patient about the various times he has been admitted and the several institutions that he has been to; he knows all the methods used and all the answers to the alcoholic problem, and he usually throws the "wet blanket" on the new patient by saying, "You'll go back to drinking and be back in a year; they all do." This is purely an alibi for his own failures, but this line of personal propaganda has to be combatted and defeated.

At this time let me say a word of praise for that fine group of alcoholics who are sincere in wanting to get well and who are most cooperative. They get well and stay well, and they are among our best citizens. They need no defense from any one. They have been sick and have recovered.

The alcoholic patient often has many physical defects, both physical and neurological, and, until these are corrected, the patient cannot be considered well or in a position to resume his occupation. The periodic alcoholic who goes on a binge every three or four weeks usually consumes large quantities of alcohol for a period of several days and stops only when he is so sick that nothing will remain in his stomach. He is

then willing for the physician to help him. These periods of near starvation are bound to produce a nutritional and vitamin imbalance of the worst type, as well as dysfunctions or disturbed functions of the stomach, such as gastritis, hepatitis, and malnutrition of brain cells, with the resultant emotional instability. Consider what will eventually happen over a period of a year or more if these periods of alcoholic forced starvation are repeated every few weeks. The individual becomes more and more addicted to the narcotic effect of the alcohol and, therefore, he more often repeats the alcoholic spree because the addiction becomes stronger. The nutritional state grows worse, the vitamin deficiency more and more pronounced, with a resulting chain of symptoms referred to the varying systems. Not the least is the change of personality that frequently results.

This is true of the steady or daily drinker who, over a period of years, consumes from a pint to a quart of whiskey daily. Changes occur in his system, a result of the nutritional imbalance resulting from the alcoholism. I am not speaking of the chronic alcoholic who is drunk daily from this amount, but I have reference to the man who drinks from a pint to a quart and who is daily at his work. It is very difficult to make these patients understand that time and proper treatment are necessary to repair or correct the physical damage that they have incurred as a result of the vitamin and nutritional changes caused by their drinking. Many research physicians and clinicians assert that the damage is a result of the inhibitory action of the alcohol on the absorption of vitamins, or that the changes occur from the impaired nutritional condition resulting from the ingestion of alcohol.

Goodhart and Jolliffe,<sup>1</sup> in their discussion of polyneuritis of alcohol and the dose of Vitamin B<sub>1</sub>, quote an article by Jolliffe, Colbert and Joffe<sup>2</sup> "in which they found that the diets of the alcoholic addict with polyneuritis failed over an effective period of time to contain an adequate quantity of

Vitamin B; and second, that the diets of alcoholic addicts without polyneuritis, though the addiction was of long duration, contained adequate quantity of Vitamin B; and third, that certain subjects without polyneuritis consumed enough alcohol over a sufficient period of time to cause peripheral nerve impairment if alcohol per se was its cause."

Jolliffe and Goodhart speak of the lack of improvement in the objective signs of motor nerve involvement after treatment and they believe it to be caused by relatively "Irreversible anatomic changes in the peripheral nerves occasioned by an acute Vitamin B<sub>1</sub> deficiency." They conclude: "Vitamin B deficiency is the primary cause of the polyneuritis of the alcoholic addict."

Piker and Cohn,<sup>3</sup> reporting on the treatment of delirium tremens cited much improvement in statistics at Cincinnati General Hospital with a treatment of spinal drainage, 50 c.c. 50 per cent glucose intravenously four to five times daily, digitalization within twenty-four to thirty-six hours, sedation using paraldehyde, and a high caloric intake supplemented by vitamins of the B group. The mortality rate was dropped to 5.3 per cent and the average hospital stay was 4.8 days. This report is based on a study of 300 consecutive cases admitted to the Cincinnati General Hospital from January 1, 1933, to July 1, 1935.

Spies, Chinn and McLester,<sup>4</sup> in their studies on "Severe Endemic Pellagra", conclude, "The signs and symptoms, the predisposing dietary insufficiency, the clinical course of the disease and the response to treatment of these patients with endemic pellagra was the same as those of pellagrins previously studied whose disease followed the chronic excessive use of alcohol, the so-called alcoholic pellagra."

Spies, Cooper, and Blankenhorn<sup>5</sup> reporting on the use of nicotinic acid in the treatment of pellagra conclude: "The lesions of the mucous membrane in 11 cases of pellagra (2 endemic pellagra, 3 alcoholic pellagra and 6 pellagras secondary to organic disease) were cured promptly by the administration of nicotinic acid."

Askey<sup>6</sup> writes: "Vitamin deficiencies in chronic alcoholism may be brought about by an inadequate diet, insufficient vitamins, deranged gastro-intestinal function (affecting both digestion and absorption) and a diminution in the volume of the gastric secretion, a diminished acidity and an increased incidence of achlorhydria." He asserts, "It is impossible to predict when clinical manifestations of pellagra or those of polyneuritis will develop in a patient with chronic alcoholism." He stresses the multiple vitamin deficiencies rather than one particular vitamin and further emphasises the necessity of a high protein diet as well as vitamins.

Jolliffe, Bowman, Rosenblum and Fein<sup>7</sup> report 150 cases of an encephalopathic syndrome, a condition heretofore nearly always fatal, which they believe was caused by nicotinic acid deficiency. The above authors quote Bender and Schilder who describe the clinical picture as one of a group of five which they called "encephalopathia alcoholica". Their classification of the type of alcoholics encephalopathia was related to the most pronounced manifestations: No. 1, Clouding of consciousness and changing rigidities. No. 2, Cerebellar symptoms. No. 3, Catatonia. No. 4, Alcoholic delirium. No. 5, Polyneuritis. Further in the article they state "The encephalopathic syndrome does not occur exclusively in alcoholic patients" and they quote Spies and Sydenstrecker "as having observed this syndrome in endemic pellagrins."

Foreign Letters A. M. A. reporting on the Third International Congress on Nutrition:<sup>8</sup> "In the discussions attention was urgently directed to the extremely harmful effects of chronic alcoholism biologically, morally, and socially on the under-nourished populations."

Conclusions by Spies and Vilter on Vitamin E:<sup>9</sup> "Our findings suggest that an injection of synthetic alphatocopherol is effective temporarily in relieving neuromuscular symptoms, roaring sensations in the ears, anorexia and insomnia in selected persons with malnutrition, but with no



clinical evidence of pellagra, beriberi or riboflavin deficiencies."

Kiene, Streitweiser and Miller<sup>10</sup> in their paper state that their primary purpose was to prove that alcohol is not the principal factor in the production of delirium tremens and that a deficit of Vitamin B<sub>1</sub> content in the brain parenchyma is chiefly responsible. A central neuronitis, an irritative phenomena, is caused by a perverted carbohydrate and Vitamin B<sub>1</sub> relationship, which when treated with adequate Vitamin B<sub>1</sub> responds more remarkably, as far as subsidence of symptoms is concerned, than do the peripheral states of polyneuritis of alcoholic origin.

Robinson and Shelton,<sup>11</sup> reporting on the use of insulin, glucose and thiamine chloride in the treatment of acute alcoholism, base their treatment on the belief that alcoholism is a disease with a chronic progressive pathological background, characterized by successive acute pathophysiologic episodes which have primarily a nutritional background.

An editorial in the A. M. A.<sup>12</sup> states that Jolliffe has shown that the rather narrow margin of safety in the modern American diet with respect to the adequacy of Vitamin B<sub>1</sub> can be greatly decreased or largely erased by the consumption of alcohol, since the metabolism of the alcohol calories increases the need for thiamine which the alcohol itself cannot provide.

Jolliffe<sup>13</sup> concludes from his studies that (a) no alcohol addict with an estimated adequate vitamin intake had polyneuritis and (b) every alcohol addict with an estimated absolute deficiency of Vitamin B for twenty-one days or more had polyneuritis. Polyneuritis may develop as early as the seventh day in an alcohol addict of estimated vitamin deficiency.

Queries and Minor Notes A. M. A.<sup>14</sup> has this to say: "Vitamins in chronic alcoholism. Strictly speaking vitamin therapy is not a treatment of alcoholism, but is frequently of value in the treatment of the hypo-avitaminosis that accompanies chronic alcoholic addiction. This lack of vitamins is chiefly the result of the failure of

the addicts to eat sufficient vitamin containing food. While the failure results in a lack of the food contained vitamins, the most common clinical indication of vitamin lack is the occurrence of peripheral neuritis."

Alexander<sup>15</sup> describing the changes in the nervous system of chronic alcoholics states "The majority of pathological conditions encountered in the nervous system in chronic alcoholism are attributable to associated vitamin deficiencies, particularly Vitamin B<sub>1</sub>, nicotinic acid and Vitamin C."

Bean, Spies and Blankenhorn<sup>16</sup> in writing on pellagra in Ohio Hospitals state, "In alcoholic pellagra the vitamin wants have not been satisfied because the beverage alcohol, the chief source of calories, ordinarily contains none and the diet does not make up the deficit."

Strecker and Rivers<sup>17</sup> report the results in 133 cases of alcoholic toxic states with 100 c.c. 50 per cent dextrose, 30 units of insulin and 100 mgs. of thiamine hydrochloride. This can be repeated in three hours if necessary. Results were excellent.

Cannon, Modarelli, DeVincenzo and Swiney<sup>18</sup> report, "The treatment of 15 cases of delirium tremens with an intravenous injection of 50 c.c. of 50 per cent glucose, 8 c.c. of Vitamin B<sub>1</sub>, approximately 25000 units, and 25 units of insulin as soon as the diagnosis is made. In the majority of cases only one injection is necessary. The improvement is due to a decrease in cerebral edema as well as to supplying the vitamin deficiency and the increased nutrition for the brain contained in the glucose."

The work of Spies and his co-workers<sup>19, 20</sup> on Vitamin B<sub>6</sub> has been most significant. The application of this knowledge will greatly benefit many cases of the B complex group deficiencies.

I call your attention to the publication "The Role of Nutritional Deficiency in Nervous and Mental Disease," a report of the Association for Research in Nervous and Mental Disease, proceedings of the Association 1941 meeting,<sup>21</sup> and especially those articles by Russell Wilder, W. H. Sebrell, Tom D. Spies, et al, Karl Bowman

and Herman Wortis and James M. McLester. This treatise is highly instructive from the first to the last page.

Berry<sup>22</sup> reporting gastroscopic studies on 100 persons of unquestionable chronic alcoholism gave 30 per cent showing no gastritis, 35 per cent showing a mild chronic superficial gastritis and 35 per cent to have an unequivocal chronic gastritis. My observations indicate that these figures are substantially correct.

Isaac J. Silverman<sup>23</sup> reports on the use of hypertonic saline solution in the treatment of the alcoholic psychosis with very good results. He mentions this treatment in the psychosis of alcoholic pellagrins and these responded nicely, even though the vitamins were withheld, but used later on in the rehabilitation.

In this group of 2275 cases I have not seen one case of delirium tremens. I have seen many cases of alcoholic hallucinosis and many cases of alcoholic or toxic psychosis but not one case of delirium tremens.

In hallucinosis and psychosis vitamins in large doses, along with hypertonic 50 per cent glucose are used immediately. I occasionally use 5 units of insulin at the same time, never over 10 units of insulin. I prefer the B complex preparations and reinforce them with the thiamin or nicotinamide. This is given intravenously once in twenty-four hours but the glucose and insulin can be repeated in four to six hours. Vitamins by mouth are also given in large doses, as well as a high proteid diet and one that is readily assimilable and one that the patient will take readily, such as egg-milk, with two or three eggs well beaten and flavored with vanilla given every two or three hours. Protein foods are given freely and insisted on. Magnesium sulphate in large doses acts very well and in my opinion has a definite place in the treatment of these cases.

On two occasions I have used the saline solution as suggested by Silverman and found the results satisfactory where the vitamin and insulin method had produced an improvement but had not cleared the

condition of hallucinosis. This was really a combination of the two methods.

Vitamin C has been reported as being lowered in the blood and spinal fluid of these alcoholic psychoses. I have not seen any appreciable effect on the cases of large doses, either intravenously, subcutaneously or orally.

Pellagra is seen frequently, beriberi more often than one would suspect, and moderately severe secondary anemias are not infrequent in the alcoholic patient and are not a result of the alcohol per se but a result of the state of malnutrition resulting therefrom.

Late investigations and studies on alcoholic cirrhosis are proving conclusively that these hepatic changes are due to a deficiency disease and most probably the B complex group associated with a low protein intake. The early diagnosis of liver damage has been greatly facilitated by improved laboratory technics, and therefore, early treatment is possible. The use of methionine and choline and proper diets and other therapeutic measures will prevent many of the cases of alcoholic hepatitis from progressing to a cirrhosis.

I would call attention to a severe acidosis that does occasionally develop as a result of the starvation. Hartmans solution acts well in these cases and rarely does it have to be repeated. Dextrose 5 per cent with sodium lactate has also been used with good results.

Advancement in the treatment of the alcoholic during the past decade has been in great part due to advancement in our knowledge of nutrition. Every advance by the nutritional specialist or research worker in this field adds another something to our armamentarium in treating the alcoholic. He is a nutritional guinea pig of his own making. It remains for psychiatrists to apply the knowledge passed on to us by the nutritional experts to help the alcoholic to regain his health.

This writer believes from clinical observation that a powerful narcotic, such as alcohol, when used excessively, will produce an addiction of varying intensity in the sus-



ceptible patient. The various addiction diseases deserve special studies along this line. Basically there is no difference between the opium group addicts and the alcoholic addict. The mechanism of addiction is the same and the abrupt withdrawal symptoms may be very stormy in both types. The craving or desire can be very strong in the alcoholic. The addiction phase of these cases has not been stressed sufficiently.

A great deal has been said and written about will power or volition. My opinion is that it is only good or strong when the nervous system has regained its stability; therefore, the alcoholic is not in a position to remain well until his nervous and emotional stability has been restored and the proper insight given by psychiatry.

I would call your attention to the fact that alcoholism may be a result of organic brain disease. We all know that this is a frequent fact in neurosyphilis. This writer in 1935<sup>24</sup> reported alcoholism as a symptom of Von Economo's encephalitis. In this article I am presenting in tabulated form the spinal fluid findings in 15 cases with characteristic cell-globulin dissociation, increased globulin, negative colloidal gold, and Wasserman. This is true in all cases

except one and in this particular case the cells were elevated and changes were found in the colloidal gold test. The clinical symptoms were mostly in the emotional sphere plus alcoholism. It is my opinion that alcoholism uncomplicated by any inflammatory brain disease does not show spinal fluid changes. This viewpoint holds for avitaminosis. Kaplan<sup>25</sup> states that the serology of chronic alcoholism is negative. Alpers<sup>26</sup> also states: "The spinal fluid is normal in chronic alcoholism." Merrit and Fremont-Smith<sup>27</sup> state: "The cerebrospinal fluid is usually entirely normal in cases of polyneuritis associated with acute and chronic alcoholism." These cases are presented for your consideration. The author thinks they are chronic types of Von Economo's encephalitis with alcoholism as a symptom.

The neurological manifestations of the peripheral nervous system are mostly covered by the neuritides. Vitamin therapy is the treatment par excellence but in the acute phase the infra-red ray does help. Where reaction of partial degeneration has set in the addition of the galvanic, sinusoidal and faradic currents is of great value and sometimes surprisingly so.

## SPINAL FLUID ANALYSIS\*

	CELL COUNT	GLOBULIN TEST	NOGUCHI TEST	PANDY TEST	SUGAR MGS. PER 100cc	TOTAL PROTEIN MGS. 100cc	GOLD COLLOIDAL	MODIFIED KOLMER WASS.
A. S. H.	1	Positive	+++	+++	60	35 mgs.	(0000000000)	Negative
C. S. A.	1	Positive	+++	+++	64	32 mgs.	(0000000000)	Negative
L. D. K.	1	Positive	++++	++++	74	50 mgs.	(0000000000)	Negative
M. B.	0	Positive	+++	+++	76	30 mgs.	(0000000000)	Negative
M. B. D.	3.1	Positive	+++	+++	56	30 mgs.	(0000000000)	Negative
J. E.	55	Positive	++++	++++	50	40 mgs.	2234432100	Negative
T. R. W.	1	Positive	+++	+++	40	30 mgs.	(0000000000)	Negative
J. G.	1	Positive	+++	+++	68	30 mgs.	(0000000000)	Negative
C. B. M.	1	Positive	+++	+++	55	25 mgs.	(0000000000)	Negative
H. P.	1	Positive	+++	++++	53	30 mgs.	(0000000000)	Negative
M. S.	1	Positive	++++	++++	71	42 mgs.	(0000000000)	Negative
T. P.	0	Positive	+++	++++	70	25 mgs.	(0000000000)	Negative
B. S.	3	Positive	++++	++++	70	56 mgs.	1222220000	Negative
W. W. B.	0	Positive	++++	++	55	55 mgs.	(0000000000)	Negative
C. L.	0.3	Positive	++++	++++	66	38 mgs.	(0000000000)	Negative

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## CONCLUSIONS

1) Every alcoholic has a psychiatric problem. This psychiatric problem varies in intensity with each case.

2) The nutritional phase is most important and improvement in this phase is often paralleled by an improvement in psychiatric symptoms.

3) Every alcoholic is an addict.

4) The vast majority of these cases should be institutionalized for study and treatment.

5) Every alcoholic given the proper help can get well and stay well, provided he accepts the fact that under all circumstances he cannot take an alcoholic drink of any type.

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## MYXEDEMA

## A REPORT OF TEN CASES FROM A GENERAL HOSPITAL

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SHREVEPORT

Hypothyroidism is a term referring to any state in which an inadequate amount of thyroid hormone is made available to the tissues. This inadequate supply of thyroid hormone may be temporary or permanent, and to a varying degree of severity. If the hypothyroidism is of sufficient degree and duration, clinical alterations appear which establish a clinical entity.

There are several types of thyroid insufficiency, which as clinical entities are in part dependent on age and in part dependent upon the means by which the thyroid insufficiency was produced. These are spontaneous adult myxedema, myxedema following thyroiditis, postoperative myxedema, and endemic myxedema or cretinism. These first four are believed to be essential results of deficient thyroid function, while endemic myxedema is believed to be a more complex disorder in which other glands in addition to the thyroid are involved.<sup>1</sup>

We will deal here with spontaneous adult

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myxedema and shall henceforth refer to it as "Myxedema".

Myxedema develops slowly and usually in patients with no previous history of thyroid disease. It occurs most frequently in females of middle life but may occur in males and other age groups. Pathologically, the only constant finding in both treated and untreated cases is atrophy and virtual absence of the thyroid gland.<sup>2</sup>

The onset is relatively insidious and first manifested by complaints of weakness, easy fatigability and sensitivity to cold. A gain in body weight is commonly found but sometimes the appetite is so poor that this does not occur. In time there follow the characteristic signs of puffiness of the eyes, dryness of the skin, a tendency for the hair to fall out and the almost complete disappearance of sweating. Menorrhagia is common but may be absent. Over a period of years the clinical condition progresses and puffiness of the tissues over the entire body appears. Speech becomes thick and the voice hoarse and deep with a low pitch. Somnolence increases and there is a marked slowness in responding to questioning. Eventually imbecility may intervene.

Laboratory examinations will usually show a high blood cholesterol; and an anemia, either of the hypochromic or macrocytic type, is commonly found. Hypochlorhydria or achlorhydria will be found in the majority of cases.<sup>4</sup> The urine may contain albumen and the phenolsulfonphthalein test gives low results but the renal function is not significantly impaired.<sup>5</sup> The basal metabolic rate will be low.

A particular form of heart disease is a part of the clinical picture of advanced myxedema. It is characterized by cardiac enlargement, a slow pulse rate, and reduced cardiac output.<sup>2</sup> The blood pressure is usually low but in the later stages of the disease may be elevated.<sup>8</sup> Electrocardiographic changes are present which consist of flat or inverted T waves, small P waves, and QRS complexes of low amplitude. The heart shows moderate enlargement on x-ray. Pathologically at postmortem, the myxedemic heart will show changes which

are characteristic of this condition but not specific for it.

La Due<sup>7</sup> describes three cases of myxedema which died untreated. In all three cases the heart was grossly dilated, the myocardium pale, and narrowing of the coronary arteries with atheromatous changes was found. Section of the heart muscle showed replacement of the sarcoplasm of the myofibrils by hydropic vacuoles in many places. Some of the cells were pale while others were deeply stained and had pyknotic nuclei. Stains of the vacuoles were negative for fat, mucus, and glycogen, indicating a true hydropic swelling similar to that noticed in the edematous tissues of patients with myxedema. Clinically the size of the heart and EKG findings revert to normal under thyroid therapy. The heart rate increases as does the stroke volume and if any failure is manifested originally, it disappears.

The thyroid hormone is not necessary to life since the oxidative processes of the body continue in its absence. However, in man the resting rate of oxygen consumption is reduced one-third to one-half in total absence of the thyroid hormone.

There is found a reduced rate of protein metabolism in hypothyroidism with storage of a considerable amount of protein in the interstitial fluid. The peculiar edema of hypothyroidism is thought to be due to a progressive deposit of protein in the interstitial spaces, which tends to withdraw fluid from the plasma with a resultant increase in the volume of interstitial fluid, a decrease in the volume of plasma, and an increase in the concentration of plasma protein. According to Boothy<sup>6</sup>, this consists of a semifluid albuminous substance containing about 13 per cent protein and represents an increase in the normal quantity of protein. With administration of thyroid, a diuresis takes place and a considerable portion of this protein undergoes metabolism and is excreted in the urine. However, no specific diuretic effect of the thyroid hormone can be demonstrated.

Both free and esterified cholesterol are elevated in hypothyroidism. Green<sup>10</sup>, in

a series of cases at the Lahey Clinic, reported nine patients with an average serum cholesterol level of 399 milligrams per cent before treatment with thyroid extract. These patients were given thyroid therapy and the serum cholesterol at the termination of study (when the patients were symptom-free) averaged from 120 to 250 milligrams per cent with a mean average of 180 milligrams per cent. There are exceptions to the rule and numerous cases of myxedema have been seen with apparently normal cholesterol levels. Peters and Mann<sup>2</sup> explain this by stating that some individuals normally tend to have high cholesterol values while others tend to have low values. With thyroidectomy or thyroid atrophy, these values will rise to the same extent in both individuals. However, in those individuals whose cholesterol level was initially high the rise will be accentuated, while in those individuals whose initial cholesterol level was low the rise will be partially masked. Nutrition and food intake also have a direct bearing on the cholesterol blood level and may distort and mask the picture. In cases of malnutrition, poor appetite, or any poor food intake, in spite of a hypothyroid condition the cholesterol level will be low. But, if the patient is fed by tube or given an adequate diet, the cholesterol level will rise proportionately. Steiner and Domenski<sup>9</sup> fed ten patients on high cholesterol diets for eight to ten weeks. The serum cholesterol in each increased from 50 to 218 milligrams per cent with an average rise of 101 milligrams per cent.<sup>9</sup> High cholesterol values are also found in diabetes mellitus, lipoid nephrosis, certain types of liver disease and obesity.<sup>11</sup>

Diagnosis of myxedema can only be made on the proper evaluation of clinical signs and symptoms, together with BMR and serum cholesterol values. It is important, however, to evaluate the case as a whole and not place particular emphasis or reliance upon a single procedure. The specific laboratory means of diagnosing early myxedema is the serum precipitable iodine level which is depressed in this condition and

in no other as shown by Bassett, Coons and Salter.<sup>12</sup>

The myxedematous patient, especially if the condition has been severe and of long standing, exhibits a peculiar initial hypersensitivity to thyroid extract. This is even more apt to occur in the severe cases with cardiac manifestations.<sup>3</sup> Means<sup>13</sup> states emphatically that in inaugurating thyroid therapy the physician should proceed with extreme caution and have the patient under surveillance. Thyroid extract is a cumulative drug, the full effects of a single dose being delayed for ten days.<sup>14</sup> The effects of the drug may last as long as seventy days. However, we may assume that therapeutic effects will have passed off in about thirty days.

When giving thyroid it is well to give it by the cumulative plan. This involves giving a small amount at the beginning, at such intervals so as to build up a concentration in the body adequate to produce a therapeutic effect. For proper evaluation of the dosage we must know when the peak effect of a single dose is reached and when the maximum therapeutic level is attained. Goodman and Gilman<sup>14</sup> state that the final decision regarding a given dose level of thyroid cannot be reached until the patient has been treated for several weeks. The

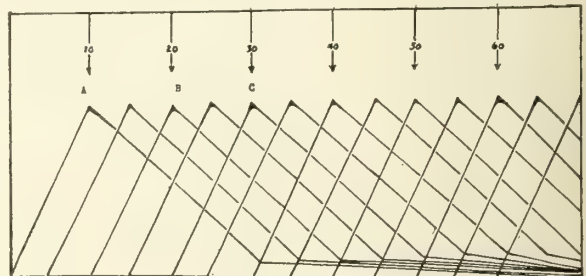


Fig. 1

Legend: Schematic graph illustrating the cumulative effect of repeated single doses of thyroid extract; letter A represents the time interval required for the maximum effect of a single dose of thyroid extract; letter B represents the time required from onset of dosage to obtain the maximum cumulative therapeutic effect; letter C represents the point of elimination of the first single dose of thyroid extract. The time interval is represented in ten day periods by arrows at the top of the chart.



following graph will clearly illustrate this point. Thus the full effect is obtained about the third week when we have summation of the waning effect of the first dose plus the various stages of effect of other single doses.

It has been found that overdosage or too rapid dosage of thyroid extract in cases of long standing myxedema may produce serious results. Anginal attacks have been reported as well as arrhythmias and death.<sup>2, 8</sup> Aisner<sup>16</sup> reports a case of complete heart block resulting from excessive dosage of thyroid extract, while cases of bundle branch block and auricular fibrillation have been also reported.<sup>17</sup>

We here report two cases in which we feel the cause of death was too vigorous thyroid medication. We believe that in advanced cases of myxedema thyroid dosage should be started slowly and in small amounts, bearing in mind the fact that the cumulative effect of the drug will not be fully observed for three weeks. Duncan<sup>2</sup> recommends beginning dosage of half a grain a day for three or four days, then discontinuance of therapy for several days after which the patient should be continued on the half-grain dose. The maintenance dosage of thyroid extract should be estimated by observation of the patient and regression of symptomatology, not the basal metabolic rate or cholesterol level. The patient, accustomed to a slow way of life may feel much better when the basal metabolic rate is about minus 10 than she would if it were at zero and her metabolism more rapid.<sup>2, 8, 18</sup> Once on a comfortable maintenance dose the patient may be carried on indefinitely with no return of symptomatology. Burgess reports a case which has been maintained comfortably on thyroid extract for fifty-two years.

#### CASE REPORTS

Case No. 1. A forty-eight year old white woman entered the hospital complaining of dyspnea, anorexia and weakness. Her illness dated back seven years when she first noticed dryness of the skin and loss of hair, followed by huskiness of the voice, difficulty in speaking, and a general inability to get things done.

Physical examination revealed an obese, drowsy, middle-aged female. The face was heavy, pallid

and expressionless, and there was a moderate amount of periorbital edema present. The voice was husky and speech halting. The skin was dry and scaly and the subcutaneous tissue was thickened but did not pit on pressure. Examination of the heart, lungs, and abdomen revealed no abnormalities. The blood pressure was 215/140.

Laboratory studies revealed a normal blood picture, a serum cholesterol level of 500 milligrams per cent, BMR's of minus 24 and minus 26 and achlorhydria.

The patient was placed on 4 grains of thyroid extract daily on the fifth hospital day. On the ninth hospital day the patient complained of headache. On the eleventh day the headache was more severe and she was nauseated and vomiting. The patient expired on the seventeenth hospital day.

Necropsy revealed marked arteriosclerosis, thyroid atrophy and an enlarged edematous heart. No anatomical cause of death could be found but it was felt that death had resulted from the excessive thyroid medication.

Case No. 2. A seventy year old white female entered the hospital complaining of easy fatigability, gradual gain in weight, and malaise for five years duration.

Physical examination revealed an obese white female with dry scaly skin and a hard non-pitting edema over the entire body. Examination of the heart, lungs, and abdomen revealed no abnormalities. Laboratory studies revealed a mild anemia, a serum cholesterol level of 290 milligrams per cent, and BMR's of minus 27 and minus 23.

The patient was placed on 2 grains of thyroid extract a day and maintained on this dosage for twenty days, at which time she began to evidence signs of toxicity, precordial pains and lethargy. In spite of this the thyroid dosage was raised to 6 grains a day and maintained at this level for fifteen more days. During this time the patient became increasingly toxic and complained of pain in the head and chest. The thyroid was discontinued on the thirty-fifth day after medication was started. A serum cholesterol level taken the day before exitus was minus 59 milligrams per cent.

It was felt that the cause of the patient's death was excessive dosage of thyroid extract.

We feel that the death of both of these patients was directly attributable to excessive dosage of thyroid extract. They were both started on what we consider massive dosage. The first patient received 4 grains of thyroid extract a day which was continued until exitus in spite of the development of the general symptoms of toxicity which should have suggested to the physician the discontinuance of the drug. The second patient first received 2 grains of thyroid extract; however, this dosage

was shortly raised to 6 grains a day. This patient developed definite symptoms of toxicity which were recognized and although thyroid medication was discontinued she had already received enough of this slowly excreted drug to cause her death.

Case No. 3. A twenty-eight year old white female entered the hospital complaining of menorrhagia, generalized weakness, and malaise of one year's duration. She had also noticed a generalized swelling of the body, particularly the face.

Physical examination revealed an obese white female with dry scaly skin and periorbital edema. Examination of the heart, lungs, and abdomen showed no abnormalities. The blood pressure was 80/60. Blood studies revealed a slight anemia. BMR's were minus 41 and minus 46.

The patient was placed on 4 grains of thyroid extract a day on the fifth hospital day and maintained on this dosage for twenty-one days, after which she was discharged on 2 grains a day. At this time she showed marked clinical improvement and her BMR was minus 19.

Case No. 4. A thirty-two year old colored female entered the hospital complaining of weakness, menorrhagia, and lassitude of seven years duration. She had also noticed falling out of her hair and puffiness of the face.

Physical examination revealed an obese colored female with a puffy appearing face, dry scaly skin, and coarse scanty hair. Examination of the heart, lungs, and abdomen showed no abnormalities. The blood pressure was 90/60. Laboratory studies revealed a slight anemia, a serum cholesterol level of 300 milligrams per cent, and BMR's of minus 37 and minus 29.

The patient was placed on 1 grain of thyroid extract a day and maintained on this dosage for eleven days. During this time she showed some clinical improvement. However, she signed out of the hospital on the eleventh day and no follow-up could be made.

Case No. 5. A fifty-one year old white female entered the hospital complaining of generalized swelling, weakness, and easy fatigability of seven years' duration.

Physical examination revealed an obese white female with thickened features, puffy face, and dry scaly skin. The voice was hoarse and speech was halting. Examination of the heart, lungs, and abdomen showed no abnormalities. Laboratory studies revealed a slight anemia, a serum cholesterol level of 260 milligrams per cent, and BMR's of minus 37 and minus 36.

The patient was placed on  $\frac{1}{2}$  grain of thyroid extract a day on the fifth hospital day. This dose was raised gradually half a grain at a time until on the thirtieth hospital day the patient was re-

ceiving 2 grains a day. The patient's course in the hospital was excellent, and on the forty-fifth day she was discharged much improved.

Case No. 6. A forty-four year old colored female entered the hospital complaining of progressive weakness and sensitivity to cold. She had noticed that her voice was becoming increasingly hoarse and that her face was swelling.

Physical examination revealed a lethargic colored female with dry scaly skin and sparsity of hair. The voice was hoarse and speech halting. A hard non-pitting edema was present over the entire body. The blood pressure was 108/80. Examination of the heart, lungs, and abdomen showed no abnormalities. Laboratory studies revealed a slight anemia, a serum cholesterol level of 292 milligrams per cent, and BMR's of minus 31 and minus 33.

The patient was started on thyroid extract,  $1\frac{1}{2}$  grains a day. The patient had an excellent hospital course and was discharged after thirty days on the same dosage of thyroid extract.

Case No. 7. A sixty year old white female entered the hospital complaining of a gradual increase in weight over the last three years accompanied by puffiness of the face and increasing hoarseness.

Physical examination revealed an obese white female with coarse hair, a dry scaly skin and puffy face. The voice was hoarse and speech halting. Examination of the heart, lungs, and abdomen showed no abnormalities. The blood pressure was 120/75. The serum cholesterol was 427 milligrams per cent and the BMR's were minus 27 and minus 23. The electrocardiograms showed a diphasic T1 and T4, low amplitude T2 and T3, and low voltage QRS complexes in all leads.

The patient was placed on 1 grain of thyroid extract a day on the second hospital day. On discharge sixty days later the patient felt much better and symptomatology had completely regressed.

Case No. 8. A fifty year old white female entered the hospital complaining of gradually increasing weakness, fatigability and sensitivity to cold.

Physical examination revealed an obese white female with puffy face, dry scaly skin and sparse hair. The voice was deep and hoarse and speech halting. Examination of the heart, lungs, and abdomen showed no abnormalities. The blood pressure was 90/60. Laboratory studies revealed a mild anemia, serum cholesterol levels of 325, and 312 milligrams per cent, and BMR's of minus 17.

The patient was placed on thyroid extract, 1 grain daily. Her course in the hospital was excellent and she was discharged in nineteen days, showing much symptomatic relief.

Case No. 9. A sixty-six year old white female entered the hospital complaining of gradual increasing weakness, fatigability and sensitivity to cold.

Physical examination showed an obese white female with edematous face, dry, scaly skin, sparse



hair and coarse features. The voice was hoarse and speech was halting. Examination of the heart, lungs, and abdomen showed no abnormalities. The blood pressure was 180/104. Laboratory studies revealed a serum cholesterol level of 506 milligrams per cent and a BMR of minus 24. The electrocardiogram showed inverted T waves and low amplitude QRS complexes in all four leads.

Thyroid extract, 1 grain a day, was started and continued throughout the patient's course in the hospital. The patient's recovery was excellent and she was discharged after forty-five days with complete regression of symptoms.

Case No. 10. A forty-eight year old white female entered the hospital complaining of progressive weakness, fatigability and sensitivity to cold. She also complained of gain in weight and swelling of the face.

Physical examination revealed a lethargic, obese white female with coarse features, facial edema and dry scaly skin. The voice was hoarse and speech halting. Examination of the heart, lungs, and abdomen showed no abnormalities. The blood pressure was 130/90. Laboratory studies revealed a slight anemia, serum cholesterol levels of 211 and 244 milligrams per cent, BMR's of minus 23, minus 33 and minus 33, achlorhydria, 35 per cent P. S. P. excretion and urine concentration of 1.025. The electrocardiogram showed inverted T waves and low amplitude QRS complexes in all four standard leads. X-ray of the chest showed slight generalized cardiac enlargement.

The patient was placed on half a grain of thyroid extract a day for twelve days after which the dose was raised to a grain a day. The patient was observed in the hospital while on this dosage for three weeks, and then discharged on a grain a day maintenance dose. Her course in the hospital was excellent and she left after complete regression of symptoms although her BMR was still minus 17.

#### CONCLUSIONS

In the study of 126,000 admissions at Shreveport Charity Hospital in the last nine years, 10 cases of myxedema were found. These occurred entirely in females in the middle years of life, and were confined in a majority of cases to the white race.

Thyroid extract has a cumulative effect, the full therapeutic value of the drug is not reached until at least three weeks after the start of administration and the drug is not fully excreted until at least three weeks after being discontinued.

Thyroid extract when given in excessive

dosage may cause cardiac complications and death.

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### HUMAN EQUINE ENCEPHALOMYE- LITIS, EASTERN TYPE, IN LOUISIANA

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NEW ORLEANS

The first human case of equine encephalomyelitis in Louisiana, due to the eastern type virus was reported in 1946,<sup>1</sup> and in 1947 there were ten proven cases. This disease has been reported only in the United States within the last decade. The first outbreak occurred in Massachusetts in 1938,<sup>2</sup> and Fothergill and associates,<sup>3</sup> and Webster and Wright,<sup>4</sup> isolated the eastern type of equine encephalomyelitis virus from the brain tissue of children dying of the disease, thereby establishing the etiology. In the following year, McAdams and

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Porter<sup>5</sup> isolated the virus from the brain of an adult who succumbed to the disease. Since the Massachusetts outbreak, the only other cases reported, except those from Louisiana, were three cases from Texas in 1942,<sup>6, 7</sup> and three in 1947,<sup>8, 9</sup> all confirmed by the presence of neutralizing antibodies in the blood.

On September 8, 1947, the Louisiana State Department of Health was notified that two children from the same family residing in Southwest Louisiana had been admitted to New Orleans Charity Hospital where a tentative diagnosis of encephalomyelitis had been made. Members of the Health Department investigated the cases and found that both children were acutely ill with symptoms typical of encephalomyelitis. The following day one of the children died. Autopsy was performed and part of the brain and cord tissues were frozen, part placed in buffered glycerol solution, and sections of all tissue taken for microscopic examination. The eastern type virus was isolated from the brain tissue.

Three days later, the other child expired and by this time several other suspected cases had been admitted to the Charity Hospital in New Orleans and the Charity Hospital in Lafayette, La. At the request of the State Health Officer, the United States Public Health Service sent an epidemiologist, and a veterinary pathologist, to aid in the investigation. Accompanied

by an entomologist of the Health Department this so called "encephalomyelitis team" visited the affected area, investigated some of the cases and collected insects, and specimens of blood from contacts and various animals. The results of these studies will be published by them later.

During 1947, the Health Department has had the opportunity to study 32 cases which were reported as suspected of having equine encephalomyelitis. Of these, 22 were found to be due to other diseases such as tuberculosis, meningitis, tonsillitis, mumps, etc., and 10 definitely diagnosed as equine encephalomyelitis, eastern type, (Table 1). The eastern type virus was isolated from the brain tissue of 2 cases, 7 showed positive neutralizing antibody tests, 1 positive complement fixation test, and 7 showed pathognomonic lesions in the brain tissue on microscopic examination. (Table 2) Of the 10 cases, 7 died and 3 recovered, the case fatality rate being 70 per cent.

The age distribution of cases which occurred in Louisiana substantiates the theory that children are more susceptible than adults. All, except one, were in children, from 7 months to 15 years of age. An unusual case in the series was that of a colored male, age 74 years, who developed severe symptoms and died within five days after onset of the disease. The cases were rather evenly distributed among the sexes, 6 occurring in males, and 4 in females.

TABLE 1  
SUMMARY OF HUMAN CASES

Patient	Address	Age	Sex	Color	Date of Onset	Date of Death	Date of Discharge
H DeM.	Maurice, La. #1	5	M	W	9- 2-47	9-12-47	
E. DeM.	Maurice, La. #2	2	F	W	9- 4-47	9- 9-47	
J. D.	Delcambre, La. #3	74	M	W	9-12-47		
F. J.	Weeks Isle, La. #4	15	F	C	9-16-47		10-15-47
E. DeR.	Weeks Isle, La. #5	11	F	W	9-17-47		10-19-47
M. I. S.	Franklin, La. #6	7 Mo.	M	C	9-23-47	11-16-47	
A. L.	Bay St. Louis, Miss.	3	F	W	10- 4-47	10-28-47	
L. S.	Cut Off, La. #7	4	M	W	10- 9-47	10-13-47	
M. R.	Gibson, La. #8	5	M	W	10-19-47	10-21-47	
A. B.	Theriot, La. #9	5	M	W	10-23-47		12-11-47



TABLE 2  
EQUINE ENCEPHALOMYELITIS, EASTERN TYPE VIRUS  
DIAGNOSTIC FINDINGS

Patient	Virus Isolation (Brain)	Neutralizing Antibodies (Blood)	Complement Fixation Test (Blood)	Microscopic Pathology
H. DeM.	Negative *2, 3	WEAKLY POSITIVE *3	Negative *4	POSITIVE *5, 6
E. DeM.	POSITIVE *1, 2, 3 (Eastern Type)	WEAKLY POSITIVE *3	Negative *4	POSITIVE *5, 6
J. D. <i>III</i>	POSITIVE *2, 3 (Eastern Type)	Negative *2, 3	Negative *4	POSITIVE *5
F. J.		POSITIVE *2, 3	POSITIVE *	
E. DeR.		POSITIVE *3	Negative *4	
M. I. S.	Negative *2, 3	POSITIVE *3	Negative *4	POSITIVE *5, 6
A. L.	Negative *2, 3	Negative *3	Negative *4	POSITIVE *5, 6
L. S.	Negative *2, 3	POSITIVE *3	Negative *4	POSITIVE *5, 6
M. R.	Negative *2, 3	Negative *3	Negative *4	POSITIVE *5, 6
A. B.		POSITIVE *2, 3		

\*Laboratories performing tests:

1. Donaldson, P., and Shaffer, M. S., Tulane University, School of Medicine, New Orleans, La.
2. Dascomb, H. E., and Syverton, J. T., L. S. U. School of Medicine, New Orleans, La.
3. Howitt, B. F., U. S. P. H. S., Virus Laboratory, Montgomery, Ala.
4. Hammon, W. McD., Hooper Foundation, San Francisco, Calif.
5. Dent, J., Tulane University, School of Medicine, New Orleans, La.
6. Hauser, G. H., La. State Department of Health, New Orleans, La.

TABLE 3  
HUMAN CASES  
AGE AND SEX

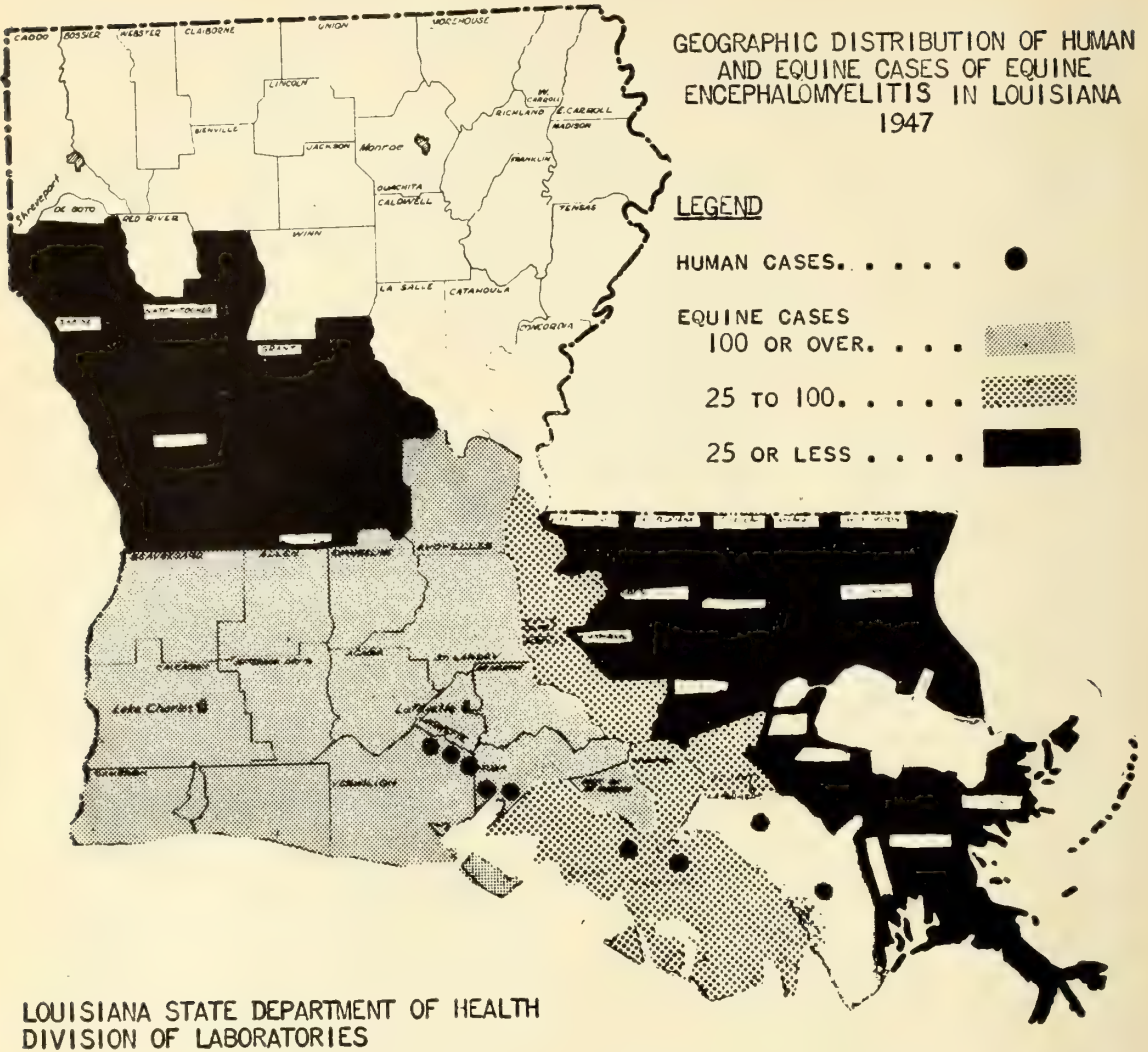
Age	Male	Female	Total	Percent- age of Total
Under 1	1	0	1	10
1-4	1	2	3	30
5-9	3	0	3	30
10-15	0	2	2	20
74	1	0	1	10
Totals	6	4	10	100

The first case was reported on September 8, 1947, and the last case on October 23, 1947. The disease appears to occur characteristically in the late summer and autumn. Nine cases reported in January and February, 1948, as suspicious of equine encephalomyelitis, have proved negative to date. In a field study, of the area from which these cases originated, only three mosquitoes and one hog louse were collected, probably due to severe cold weather. As all suspected cases and the areas from which they originate are investigated by

the State Department of Health, it is imperative that physicians throughout the state report any suspected case.

Figure 1 shows the geographic distribution of human cases of equine encephalomyelitis which occurred during the 1947 outbreak. It will be noted that most of the human cases occurred in rural areas or small towns. The map also shows the relation of human cases to equine cases, based on statistics as collected by Piercy<sup>10</sup> from a questionnaire sent to all practicing veterinarians in the state. Accurate figures on the incidence of the disease in animals vary widely, and those of Piercy are very much higher than those of the U. S. Department of Agriculture. It appears that many animal cases are never reported.

As the Massachusetts and Louisiana outbreaks are the only two known to be caused by the eastern type virus, it is interesting to compare our findings with those reported by Feemster<sup>2</sup> and Getting.<sup>11</sup> Statistically, they were quite similar. The distribution among the sexes was rather even and children were particularly susceptible in both



of the outbreaks. Seventy per cent of our cases and 70 per cent of the Massachusetts cases were in children under ten years of age. The case fatality rate in Louisiana, in humans, was 70 per cent, while in Massachusetts it was 74 per cent.

Two of the fatal cases in the Louisiana outbreak were from the same household and two other members from the family showed neutralizing antibodies in their blood. This may be of epidemiological significance as multiple cases in the same household were not present in the Massachusetts outbreak. This also raises a possibility of contact infection or vector transmission of the disease from one human to another, although laboratory experiments by various workers have failed to show

transmission of the disease by direct contact.

A summary of the clinical symptoms shows that in most cases the onset was sudden with anorexia, irritability, vomiting, sometimes diarrhea, headache, fever, drowsiness and restlessness followed by muscular twitchings, convulsions, and coma. There was rigidity of the neck and stiffness of the back, lower, and upper extremities. Most of the cases were admitted to the hospital from two to five days after onset of illness. Temperature usually ranged from 102° to 106.4° F.

Laboratory findings were rather constant. Blood examination usually showed slight leucocytosis with increase in polymorphonuclears. Blood chemistry (Sugar



and N.P.N.) and urinalysis in most cases were negative. Spinal fluid was clear or slightly hazy in appearance, while pressure, cells, and globulin showed an increase. The polymorphonuclears predominated in the spinal fluid early in the disease, and later the lymphocytes. Blood and spinal fluid cultures were negative for bacterial infection.

In the cases in which recovery took place, symptoms were not as severe, but convalescence was prolonged. One of the distressing features of the disease is that nearly all cases that recover show disabling mental and physical sequelae which are progressive in character. A study by Getting<sup>11</sup> of the 9 surviving patients of the Massachusetts outbreak, approximately one year after onset of illness, showed that 6 suffered disabling sequelae. Feemster,<sup>12</sup> in a nine year study of these cases, reports that not only have these patients shown no further improvement, but that some of the individuals have shown further retardation.

In the fatal cases, the patients grew progressively worse despite chemotherapy and supportive measures, with almost continuous convulsions and coma until death, which usually occurred from two to ten days after onset. One unusual case was that of a 7 month old colored child who died on the fifty-fourth day of illness.

Autopsies were held on the 7 fatal cases. Grossly, the brain and spinal cord showed congestion and marked edema. One case showed areas of hemorrhage. The convolutions of the brain were markedly flattened. Microscopic examination showed more or less similar findings throughout the brain tissue, most marked in the mid-brain. These consisted of diffuse infiltration of polymorphonuclear leucocytes, and a lesser number of large mononuclear cells, especially about the blood vessels, in the brain, cord and meninges; small focal areas of polymorphonuclears with abscess formation, destruction of nerve cells, with infiltration of polymorphonuclears and large phagocytic cells (Neuronophagia), many Gitter cells, areas of focal necrosis, proliferation of glial cells, with production of

glial nodules, and irregular areas of demyelination with no relation to the blood vessels. The blood vessels showed proliferation of the lining endothelium, with numerous thrombi in the small vessels, many of which were hyalinized. The walls of the blood vessels showed infiltration of polymorphonuclears with necrosis present. In cases dying after prolonged illness, only a small amount of polymorphonuclear infiltration was present with a greater amount of mononuclear invasion, marked gliosis, atrophy, and cystic changes. Changes in the viscera included congestion, proliferation of the lining of the small vessels, with numerous thrombi, interstitial pneumonitis, and incidental secondary pathological changes.

The diagnosis of encephalomyelitis is usually made clinically and confirmed by laboratory methods. The laboratory procedures of value, to confirm the diagnosis, are: (1) Isolation of the virus, (2) tests for neutralizing antibodies, (3) complement fixation test, and (4) post mortem examination.

1). Isolation of virus: Specimens of blood and spinal fluid should be collected as soon as the disease is suspected, frozen at once, and forwarded to the laboratory for virus isolation.

2). Test for neutralizing antibodies: A specimen of blood should be taken in the early stage of the disease and subsequent specimens at weekly intervals. An increasing titer of neutralizing antibodies during the course of the disease is of great value in confirming the diagnosis.

3). Complement fixation test: This has proved of little value in cases that succumbed after a few days' illness. However, in those that live over two weeks or in those that recover, it may be helpful.

For neutralizing antibody and complement fixation tests, withdraw 10 c.c. of blood by venipuncture, allow to clot, and send to the laboratory at once. If it is to be shipped a long distance, the serum should be separated from the clot.

4). Post mortem examination: In case of death, an autopsy should be performed. It is important that sections of the brain,

and spinal cord be obtained, special care being taken to obtain portions of the mid-brain. Part of the specimen should be frozen at once, and the remainder placed in buffered glycerol solution.

It should be forwarded to the laboratory for animal inoculation in an effort to isolate the virus. In cases that have succumbed early, the virus can usually be isolated from the brain tissue; whereas, in cases that have been prolonged, the virus is hard to isolate and appears to have burned itself out. Upon isolation of the virus, the type must be determined by animal protection tests.

Sections of all tissues should also be taken and placed in 10 per cent formalin for microscopic examination.

Complete epidemiology of this disease has not been established. The eastern type virus of equine encephalomyelitis was originally isolated by Ten Broeck and Merrill<sup>13</sup> from the brains of horses dying of the disease along the Atlantic Coast. Transmission of the eastern virus to experimental animals by the bite of infected mosquitos, was first reported by Merrill, Lacaille and Ten Broeck<sup>14</sup> in 1934. In 1938, Fothergill and Dingle<sup>15</sup> isolated the eastern strain virus from a wild pigeon in Massachusetts, and Tyzzer and associates<sup>16</sup> the virus from two wild pheasants in Connecticut. The same year Ten Broeck<sup>17</sup> found neutralizing antibodies present in the sera of fowls from farms, where horses had died of encephalomyelitis, and the following year (1939)<sup>18</sup> postulated that "birds act as reservoir hosts for the virus." Davis<sup>19</sup> has presented experimental evidence that birds, including English sparrows, pigeons, and cowbirds can be infected with the virus, by the bite of infected mosquitoes.

From all the evidence at hand, it appears that birds are the reservoir for the virus, from which arthropods, principally mosquitoes, become infected and transfer the infection to humans, horses, birds, and other animals.

A mosquito survey made in Massachusetts<sup>20</sup> following the 1938 outbreak showed 21 species of *Aedes* present, 6 of which had

previously been proved to transmit the eastern type virus. In a mosquito survey in Louisiana made by the Louisiana State Department of Health during 1947, 16 species of *Aedes* were found, 5 of which have been previously proved to transmit the eastern type virus (Table 4), and their seasonal incidence is shown in Figure 2.

TABLE 4  
OCCURRENCE OF MOSQUITO VECTORS OF  
EQUINE ENCEPHALOMYELITIS, EASTERN TYPE,  
IN MASSACHUSETTS—LOUISIANA

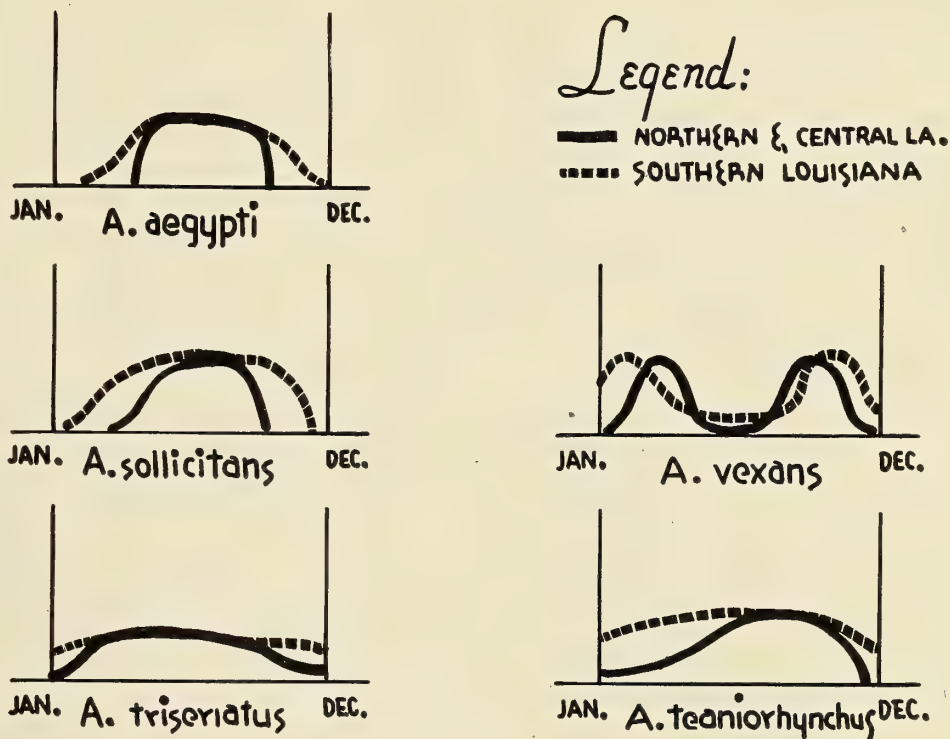
Name of Mosquito	Occurrence in Massachusetts	Occurrence in Louisiana
<i>Aedes aegypti</i>	0	X
<i>A. sollicitans</i>	X	X
<i>A. cantator</i>	X	0
<i>A. vexans</i>	X	X
<i>A. triseriatus</i>	X	X
<i>A. atropalpus</i>	X	0
<i>A. taeniorhynchus</i>	X	X
<i>A. dorsalis</i>	X	0
<i>A. albopictus</i>	0	0
<i>A. nigromaculis</i>	0	0

The prophylaxis of this disease is an important public health problem. As it has been shown that arthropods, principally mosquitoes, transmit the virus of the disease, it is important that measures be taken for their elimination. Control of mosquitoes and other insects should be carried out by proper screening of houses, barns, etc., by spraying and application of insecticides, adequate soil drainage, and destruction of breeding places. If the present concept is true, that the reservoir of the virus is in birds, elimination will present a difficult problem. Vaccination has been proved of value in animals and may be of value in preventing the disease in man.

There is no specific treatment. Serum from convalescent cases appears to be of little value, but this requires further study. General symptomatic treatment should be given.

What importance the disease will assume in the future in Louisiana is unknown. There seems to be no explanation of why the disease should remain dormant for years, then suddenly appear in new areas. Past experience, in epizootics among horses



SEASONAL DISTRIBUTION OF MOSQUITO VECTORS OF EQUINE ENCEPHALOMYELITIS, EASTERN TYPE  
FOUND IN LOUISIANA - 1947

and mules, has shown that rarely, except in a few endemic areas, does the disease recur to any extent in the same area in succeeding years. Human cases of equine encephalomyelitis usually occur only when an outbreak or epizootic of the disease is prevalent in the area, and usually after the peak in animals has been reached.

An infectious disease which has been responsible for only two proportionately small outbreaks, and a few sporadic cases in the past decade, might seem of little public health significance. However, it must be remembered that the distribution of the virus is widespread. If the present concept of the epidemiology of the disease is true, the possibility of infection in Louisiana is ever present.

#### SUMMARY

1). An outbreak of human equine encephalomyelitis, due to eastern type virus, occurred in Louisiana during 1947.

2). Ten cases were definitely proved to be of the eastern type, either by isolation of

the virus from the brain, demonstration of neutralizing or complement fixing antibodies in the blood, by typical lesions in the brain, or by a combination of the above.

3). A study of the cases shows children were most frequently affected with no special sex predilection. The disease occurred in late summer and autumn, in small towns and rural districts, especially in the area where the disease was prevalent in animals.

4). Clinically the disease was severe, usually of short duration, with high case fatality rate. The gross and microscopic autopsy findings are given.

5). Etiologic diagnosis cannot be made on clinical findings. Diagnosis depends upon the laboratory and can be established by (1) Isolation of the virus from the blood, spinal fluid or brain tissue (2) test for neutralizing antibodies (3) complement fixation test and (4) microscopic examination of tissues.

6). Complete epidemiology of equine en-

cephalomyelitis, eastern type, is not definitely established. Evidence, at the present time, indicates that arthropods, particularly mosquitoes, transmit the disease, and birds act as the host reservoir.

7). Control measures include vaccination of animals against the disease, elimination of host reservoirs and insect vectors.

The author wishes to express appreciation to Dr. Emma Moss and Dr. M. Hood, of Charity Hospital, for assistance and cooperation in collection of data and specimens, and Dr. J. Arey, of Tulane University, for furnishing some of the tissue sections and lantern slides.

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#### CHROMOMYCOSIS:

#### REPORT OF A CASE FROM LOUISIANA WITH A DISCUSSION OF ITS CLINICAL AND MYCOLOGIC FEATURES

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In spite of several relatively recent articles on the subject, chromomycosis is still a disease with which many physicians are unfamiliar. Undoubtedly the condition is not as rare as it is generally supposed to be. More probably, the lesions have been misdiagnosed and confused with granulomas similar in appearance to one or more of its varied clinical forms. This report is submitted to call attention once again to chromomycosis, to review the clinical and mycologic features of the disease and to record the first such case from the state of Louisiana.

In 1911, in Brazil, Pedroso identified the first case of chromomycosis which he called "black blastomycosis" because of the dark fungous cells of the lesions.<sup>1</sup> Lane<sup>2</sup> and Medlar<sup>3</sup> described the first case in North America in 1915. Since that time approximately 100 cases have been recorded in the world literature, nine of which have come from the United States. The cases thus far reported have originated from widely scattered areas, including the Caribbean area (Cuba, Puerto Rico and Costa Rica), Brazil and the Union of South Africa.<sup>4</sup> In the United States, cases have been recorded from Massachusetts, Texas, Missouri, North Carolina, Pennsylvania and Georgia.<sup>5</sup>

Chromomycosis has been confused on many occasions with blastomycosis. Actual-

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ly, there are definite clinical and microscopic differential features between the two diseases, so that there can be little justification for a continuation of this common error in diagnosis.

Unlike blastomycosis, the chromomycosis organism divides, not by budding, but by cross wall or septum formation, both in culture and in tissue. To point out the difference between the two diseases and to avoid confusion in nomenclature, one of us (M. M.) with de Almeida has suggested the shorter term "chromomycosis" rather than "chromoblastomycosis" by which name it has been designated in the past, thereby omitting the misleading "blasto" altogether. The prefix in "chromoblastomycosis" and "chromomycosis" has been retained by all authors as a means of indicating the pigmented nature of the causative agent.

The organism in tissue has been described by Moore and his colleagues<sup>6</sup> as spherical or irregular sclerotic cells which are thick-walled, dark brown or chestnut colored and single or multiple, appearing in clusters. The cells produce by enlargement and septum formation to form mulberry-like groups. The cells are distributed throughout the tissue in microabscesses surrounded by polymorphonuclear leukocytes or engulfed by giant cells.

It is possible to make a clinical diagnosis only in far advanced typical examples of the disease. However, if the condition is kept in mind and biopsy resorted to, the diagnosis can be established histologically with no difficulty. The condition is undoubtedly more common than has been considered heretofore. More cases will be discovered in the future if physicians are aware of the world-wide distribution of the disease.

#### MYCOLOGY

The taxonomy of the fungi causing chromomycosis (chromoblastomycosis) has been somewhat confused by the succession of new names, genera, species and varieties. Morphologically, there can be seen various structures which may be found singly or in combination in all the organisms responsible for the disease. The one undisputed

fungus, *Phialophora verrucosa* Medlar, 1915, is characterized by the production of semiendogenous spore formation through cupulliform structures termed phialophores. Other strains of fungi isolated from cases of chromomycosis have, in the past, been generally classified as *Hormodendron pedrosoi* Brumpt, 1921. The numerous isolated strains vary considerably morphologically, being characterized by the production of a variable number of large subspherical or ellipsoid, catenulate spores in acrogenous branches, the *Hormodendron* type of conidiophore; or the conidia may be arranged pleurogenously, along the conidiophore, or in head formation, the *Acrotheca* type of conidiophore; or there may be present the phialophores typical of *Phialophora*. In addition, one may find strains of organisms which have the formation of cupulliform spore bearers laterally or at the apices of the *Hormodendron* conidiophores.

Prior to the finding of the various methods of spore production and morphologic forms, the several isolated fungi were considered to be one organism and accordingly received the following names from different workers: *Hormodendron pedrosoi* Brumpt, 1921, *Acrotheca pedrosoi* Terra, Torres, da Fonseca and Arêa Leão, 1922, *Trichosporium pedrosoi* Langeron, 1929 and *Gompharia pedrosoi* Dodge, 1935.

In 1935, Carrión and Emmons<sup>7</sup> described semiendogenous spore formation in *Hormodendron*. In the same year, Moore and de Almeida<sup>8</sup> also reported all the methods of sporulation in one strain. On the basis of the various methods of spore formation and on the combination of these methods in various strains of fungi producing chromomycosis, Moore<sup>9</sup> in 1936 suggested a generic and genetic relationship of the fungi by placing the organisms in the order Phialophorae and creating three new genera, *Botrytoides*, *Hormodendroides* and *Phialoconidiophora*. In the following year, Moore and de Almeida<sup>10</sup> established their relationship in accordance with the rules of botanical nomenclature.

In an antedated publication, Negroni<sup>11</sup> recognized the need for changing the name

*Hormodendron*. On the basis of a paper presented by Moore before members of the Bacteriological Institute, Buenos Aires, Argentina, in which the genus *Hormodendroides* was discussed, Negroni created the genus *Fonsecaea* to replace *Hormodendroides* which he considered a *nomen nudum*. The name honored da Fonseca, the eminent Brazilian mycologist who was one of the early workers on the disease. Carrión<sup>12</sup> accepted the name to replace the older terms and maintained two species, *F. pedrosoi* and *F. compactum*. *Phialophora verrucosa* was considered a distinct organism. In a later paper, Carrión<sup>13</sup> upheld the genus *Fonsecaea* and discarded all other genera. Following the phylogenetic sequence proposed by Moore, Carrión created varieties to replace the genera of Moore and de Almeida. *F. pedrosoi* var. *communis* replaced *Phialoconidiophora guggenheimia*, *F. pedrosoi* var. *cladosporioides* replaced *Hormodendroides pedrosoi*, *F. pedrosoi* var. *typicus* replaced *Botrytoides monophora* and *F. pedrosoi* var. *phialophorica* replaced *Phialophora verrucosa*. The term *cladosporioides* is used by Carrión since it has been considered that *Hormodendron* is a synonym of the older *Cladosporium*.

Emmons, in presenting the mycologic report and discussion on an organism isolated from a patient with chromomycosis as published by Binford and Hess<sup>14</sup> rejected the genus *Fonsecaea* for the older name *Phialophora*. He preferred to amend the genus *Phialophora* to include, in addition to the semiendogenous spore formation, the acrogenous, pleurogenous or acropleurogenous spore formation described for *Phialoconidiophora*, *Hormodendroides* and *Botrytoides*. This seems to be a more logical choice than *Fonsecaea*. The new combinations, therefore, according to Emmons, in addition to the already accepted *Phialophora verrucosa*, would be *P. pedrosoi* and *P. compactum*. By amending *Phialophora* to include the other spore-forming types of organisms, Emmons recognized the close relationship existing between the various etiologic agents of chromomycosis as suggested by Moore, who placed all these fungi

in the order Phialophoreae. Whether all the organisms should be placed in the genus *Phialophora* is a matter which may be open to discussion. Certainly the methods of sporulation and the morphologic characteristics of *Phialoconidiophora* of Moore and de Almeida or *Fonsecaea pedrosoi* var. *communis* of Carrión would appear to merit more than synonymy with *Phialophora pedrosoi* as classified by Emmons.

The organism isolated from the case described here appears to have the characteristics of *Botrytoides monophora* or *Fonsecaea pedrosoi* var. *typicus* particularly when grown on Sabouraud's glucose agar and the characteristics of *F. pedrosoi* var. *cladosporioides* or perhaps *Hormodendroides pedrosoi* when grown on Czapek's medium. This would of course be classified as *Phialophora pedrosoi* by Emmons. On Sabouraud's glucose agar, pH 5.2, the fungus produces a colony which is compact with a central knob, concentric zones of growth, being dark olivaceous to black. The peripheral growth is dark greenish-gray to brown while the surface growth is dark mouse gray to olivaceous (Fig. 1:1). Growth is fairly rapid, attaining a diameter of approximately 3 cm. in 15 days. On Czapek's medium the colony is submerged in the agar, not compact, dark brown to black in color and attains a diameter of approximately 3 cm. in 15 days (Fig. 1:2).

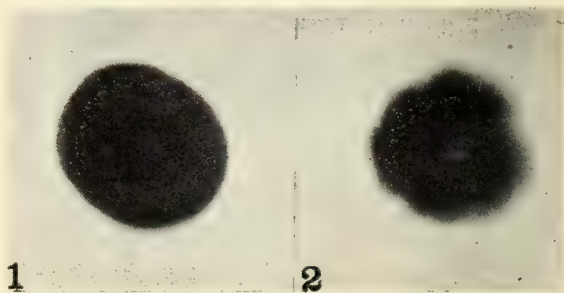


Fig. 1: 1. Colony of *Phialophora pedrosoi* on Sabouraud's glucose agar, 15 days old, actual size; (2). Colony of *P. pedrosoi* on Czapek's medium, 15 days old, actual size.

Microscopically, the fungus shows a paucity of the characteristic spore formation. On Czapek's medium the outstanding feature is the finding of brown spores, ellip-



soid to ovoid, catenulate, approximately 2-5 microns in diameter, developing from the hyphae laterally either singly or branched, suggesting the conidiophores of *Cladosporium*. Conidiophores of the *Hormodendron*

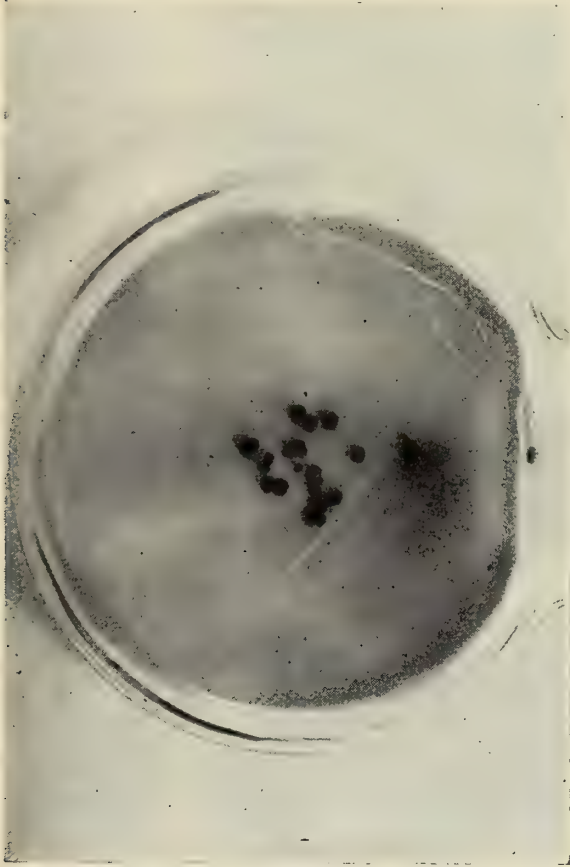


Fig. 2. Colonies of *P. pedrosoi* on Sabouraud's agar.

type may be seen, but not in great abundance and seldom attaining the development seen in other strains (Fig. 3:1-2). The conidia are subspherical to ellipsoid, catenulate in acrogenous branches, approximately 2-5 x 2-8 microns. Few conidiophores of the so-called *Acrotheca* type may also be seen. These are usually irregular, denticulate spore bearers, single or multicelled, lateral or terminal and dark brown with the conidia acrogenous or pleurogenous, ovoid ellipsoid or subfusiform, approximately 1.5-4 x 3-8 microns. On careful search, conidiophores of *Phialophora* may be found. These spore bearers, however, are rare. When observed in slide prepara-

tions they are usually simple, lateral on a hypha or occasionally branched showing two phialophores (Fig. 3:3-4). On Sabouraud's glucose agar the principal spore forming method is by the *Acrotheca* method (Fig. 3:5). The *Hormodendron* and the *Phialophora* types were not observed, although it is possible that they may be present.



Fig. 3: 1. *Hormodendron* type of conidiophores grown on Czapek's medium, X 1440; (2). Conidiophore showing acrogenous spore formation on Czapek's medium, X 1440; (3). Semiendogenous type of conidiophore (*Phialophora* type) with single small conidium on Czapek's medium, X 1440; (4). Semiendogenous conidiophore (branching form) on Czapek's medium, X 1440; (5). *Acrotheca* type of conidiophore on Sabouraud's glucose agar, X 1440.

#### CLINICAL FEATURES

The clinical varieties of chromomycosis are manifold. Of the various species of the fungus considered causative, no one

species can be correlated clinically with any particular type of lesion.

Chromomycosis occurs in the laboring classes, mostly among farmers or those in contact with farm products. In many patients the history of injury by wood or vegetation can be elicited, as is probably the case reported in this paper.

The disease apparently may occur at any age. In the cases reported to date there has been a preponderant incidence in the male sex. It appears that all races are susceptible. The disease is not considered contagious since there has been no familial spread so far reported.



Fig. 4. Chromomycosis involving the index finger.

#### TYPES

In the past, chromomycosis has been considered a disease affecting the lower extremities in the form of verrucous and granulomatous excrescences. It is now known that any part of the cutaneous sur-

face may be involved. Five clinical types have been described by Pardo-Costello and his associates.<sup>15</sup> These include:

1. The verrucous type, the form most frequently observed. This type is encountered usually on the legs in the form of papillomatous patches not unlike those seen in blastomycosis and tuberculosis verrucosa cutis. The color varies from light brown to dark red. The process tends to heal by central scarring. Suppuration is not a common feature.

2. The tuberculoid type also resembles tuberculosis verrucosa cutis as well as sarcoid. The typical lesion is a patch composed of brown hypertrophic nodules with erythematous areolas and minimal scarring. This type is considered to be an early form of verrucous chromomycosis. However, according to Pardo-Costello, the allergic response of the individual tissue to the infection may play an important role in the



Fig. 5. Same as Fig. 4. Enlarged view.



development of one or the other clinical types.

3. The syphiloid type resembles late cutaneous syphilis. The lesions are nodular, scaly and at times ulcerative, having a serpiginous, annular or arciform pattern. The process leaves a thin, depigmented scar.

4. The psoriasiform type appears as inflammatory infiltrated plaques with superimposed white, lamellated, adherent scales, similar in appearance to psoriasis.

5. The cicatricial and elephantiasic type is usually found on the leg and resembles Madura foot. This type is characterized by scarring and is considered a final stage of the disease, presenting, in addition to the scarring, verrucous lesions, scaling, ulcers and abscess formation. The elephantiasic enlargement is due to interference with the lymphatic drainage. Attacks of recurring lymphangitis are associated with this type.

#### COURSE

Chromomycosis is a chronic disease that progresses slowly, having been known to persist for as long as 40 years. There is no associated pain, pruritus or systemic symptoms in the majority of cases. Regional adenopathy is a common finding and is attributed to secondary infection. Metastases have been reported in only two cases and there have been no instances of invasion of bone. No visceral lesions have been observed. According to Pardo-Costello and his associates,<sup>15</sup> atrophy of the muscles, ankylosis and osteoporosis are common in the extremities in cases of long duration, due to immobility and scarring. The general health of patients is unimpaired. A fatal case has never been reported except when caused by some unassociated condition.

#### PATHOLOGY

Microscopically, the diagnosis can be made by finding the typical cells in the tissue. There are many features microscopically which suggest blastomycosis, tuberculosis and the mycotic granulomas

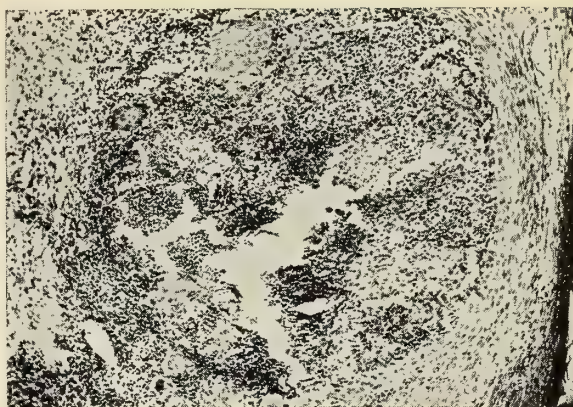


Fig. 6. Chromomycosis; supuration and necrosis in a large abscess-like formation with fibrosis and a granulomatous response around the periphery. Low power. X 135.

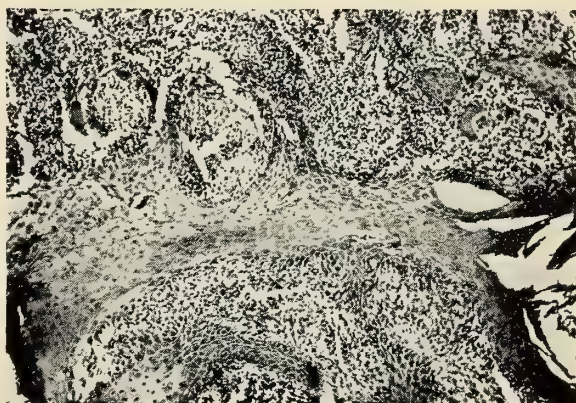


Fig. 7. Chromomycosis, showing pseudoepitheliomatous hyperplasia and microabscesses in the cutis. Low power. X 135.

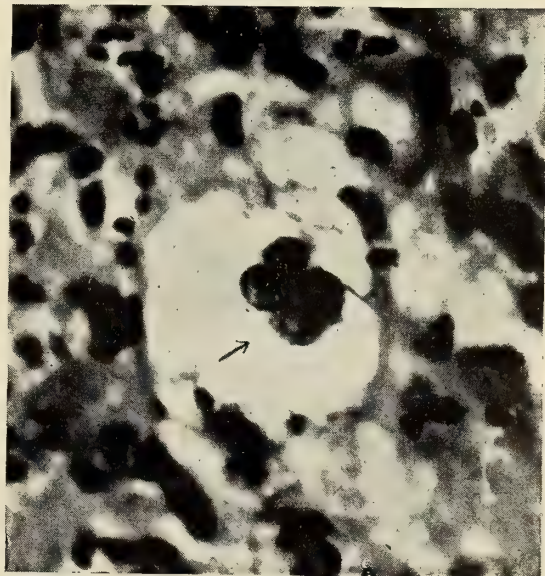


Fig. 8. Chromomycosis, showing a group of the causative organisms. High dry. X 1280.



and there are certain characteristics which serve as differentiating points. The microscopic pathology has been described in detail by Moore et al as follows: "The epidermis shows hyperkeratosis and acanthosis with a thickening, broadening and elongation of the rete pegs. Within the pegs may be seen microscopic abscesses filled with polymorphonuclear leukocytes, cellular debris and the fungous cells. At times within these areas one may also find Langhans' giant cells containing fungi. The most pronounced changes are found in the dermis. Here one sees edema, a pronounced cellular infiltration and, in older lesions, evidence of fibrosis. The cellular infiltration is made up of polymorphonuclear leukocytes, lymphocytes, epithelioid cells, plasma cells, eosinophiles and Russell's fuchsin bodies, which have been noted in tissue sections by others. Giant cells of the foreign body type or Langhans' type may be present as well as macrophages. There is sometimes a tendency to pseudotubercle formation in the infiltrate. Fibroblastic changes may occur. Necrosis and microabscesses such as are found in Gilchrist's disease are not prominent in chromomycosis. The sclerotic cells of the fungus are found scattered throughout the corium, especially in the abscesses or in giant cells. They occur either as single cells or as mulberry-like clusters."

#### DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis may be established by demonstrating microscopically, by the potassium hydroxide technic, the round, grouped, dark-colored sclerotic cells in pus, scales or sections of tissue. Cultural studies aid in reaching a diagnosis, but are not essential, since the typical cells can be demonstrated with ease and are pathognomonic of the disease.

The differential diagnosis includes blastomycosis, sarcoid, coccidioidal granuloma, maduromycosis, tuberculosis verrucosa cutis, bromoderma, syphilis, yaws, pyoderma vegetans, epithelioma, psoriasis and other diseases.

#### TREATMENT

Pardo-Costello et al.<sup>15</sup> say that roentgen therapy is of value in the treatment of the

superficial type of case and is helpful even in other cases. They recommend from 600 to 1200 roentgen units filtered through 1 or 2 mm. of aluminum. According to these authors, iodides are worthless, as are thymol, antimony, copper and the sulfonamides. They state that the treatment of choice is electrocoagulation followed by curettage, which results in a firm contracted scar after two or three months of constant care. For the cicatricial and elephantiasic type on the legs only amputation is of any avail. In general, iodides in dosage up to 90 grains daily and roentgen therapy are usually tried, sometimes with success, as in the unpublished report of Sams. Moore, Cooper and Weiss<sup>6</sup> summarize the present thought on the subject by recommending iodides, roentgen therapy, electrocoagulation or surgical excision when the lesion is small and experimental procedures when the lesion is extensive.

#### REPORT OF CASE

W. C., a white male, 81 years of age, who died on July 11, 1946, was followed at the Touro Infirmary, New Orleans, Louisiana, over a period of three years for carcinoma of the stomach and generalized carcinomatosis.

During the period from April 1945, until shortly before his death the patient was seen regularly in the hospital's dermatology out-patient department, service of Dr. R. A. Oriol, for a chronic dermatosis involving the proximal phalanx of the left index finger, of 15 months' duration. The dermatitis consisted of an erythematous plaque flush with the surrounding skin, having a slightly verrucous base without ulceration and covered with a loosely adherent white scale which tended to pile up at the border.

This condition resisted various types of local treatment as well as full doses of iodides and roentgen therapy. At the time of death, in spite of constant treatment, the dermatosis progressed slowly without at any time showing any tendency toward healing.

It was significant that the patient's occupation prior to the onset of the dermatitis consisted of working with raw wood from which barrels were constructed.

A biopsy made on September 26, 1945 was reported by Dr. J. R. Schenken as chromoblastomycosis. A description of this section of skin by Dr. Harvey Colvin was as follows: "Biopsy consists



of several small bits of skin presenting an intense chronic inflammatory and granulomatous reaction with scattered Langhans' giant cells. Pyogenic reaction is noted within the epidermis and subepidermis. Upon inspection with the high power lens, several rounded brown forms may be seen morphologically consistent with chromoblastomycetes. These sometimes occur singly but one group of four is noted together. These forms are most numerous along the edges of small pyogenic abscesses within the corium."

Scrapings from the involved area yielded the causative fungus of chromomycosis described above.

## SUMMARY

A case of chromomycosis, thought to be the first from Louisiana, is reported. The disease is discussed from the standpoint of both its clinical and mycologic features. In spite of the paucity of reports, the disease is probably not rare. It is suggested that physicians be on the lookout for further cases from this section of the country.

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## TRACHEOTOMY WITH COMPLICATION OF PNEUMOTHORAX

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Tracheotomy, even when performed as an emergency measure, is in most instances free of complications, but when they do occur trying moments are experienced by the physician. The two cases to be presented aptly demonstrate the serious complications which may ensue,—in this instance, pneumothorax, which followed tracheotomy on two children, one of whom survived, and the other expired.

Case No. 1. A seventeen months old white male was admitted to Charity Hospital with the chief complaint of cyanosis, cough, and fever. His present illness dated back three days, at which time cough and fever were first noted. The cough had become more severe with each paroxysm, with associated inability to get his breath. The day before admission, cyanosis following such a paroxysm had been noted. The cough and croup had become more pronounced, together with a loud inspiratory noise, which led the child to be admitted for treatment.

Physical examination revealed in general a toxic appearing child with a loud inspiratory croup, a spasmodic cough, and moderate intercostal and substernal retraction. The temperature was 101° F. per rectum. The pharynx was injected, with no evidence of membrane formation. The remainder of the physical examination was essentially negative. The diagnosis made at this time was acute laryngo-tracheobronchitis.

The child was placed in a croup tent, receiving steam inhalations, oxygen, and sedation of phenobarbital, supplemented with penicillin intramuscularly, and sulfadiazine orally. Six hours later no improvement was noticed, instead the respirations were more labored. Tracheotomy was deemed advisable, and over a bronchoscope, a low tracheotomy was performed. Bronchoscopy revealed a hyperemic larynx and trachea with a moderate amount of seromucinous exudate present in the tracheobronchial tree. Immediate postoperative relief was obtained. Twenty-four hours later, breath sounds over the left chest were found to be diminished along with an increase in respiratory rate. X-ray of the chest revealed a left pneumothorax and emphysema of the left lung. A water trap

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tube was inserted into the left pleura with removal of 175 cu. c.c. of air, and moderate relief of symptoms. Within twelve hours this was discontinued as the child was greatly improved. Eight days later, after an apparently normal recovery, with the tracheotomy tube being blocked eighteen hours, the tube was removed, but shortly afterwards the child began to experience severe dyspnea. An attempt was made to reinsert the same tracheotomy tube, but was unsuccessful. Therefore, again over a bronchoscope, opening the original wound, the tube was reinserted. Within twelve hours a pneumothorax again was detected on the left side after the same treatment as previously mentioned. After twelve days of uneventful recovery, the tracheotomy tube was finally removed, and the patient was discharged shortly afterwards.

Case No. 2. A white female, 2½ years of age, was admitted to Charity Hospital with a chief complaint of difficulty in breathing. The present illness dated back three days, with hoarseness the only complaint. The following day slight difficulty in breathing, and fever, had been noted, but no cough. This complaint continued to get worse until ten hours prior to admission when cough also was present.

Physical examination at the time of admission revealed in general an acutely ill child with marked respiratory difficulty, substernal and suprasternal retraction with each inspiratory effort, and cyanosis about the hands and mouth. Her temperature was 103° F. The pharynx was hyperemic, with evidence of a gray membrane on the left palatine tonsil. Otherwise, the physical examination was essentially negative. A tentative diagnosis of diphtheria was made.

Tracheotomy was deemed advisable, and over a bronchoscope, a low tracheotomy was performed, the child experiencing marked relief immediately afterwards. Bronchoscopy revealed hyperemia of the larynx with no membrane formation. One hour and a half later the child exhibited signs of air hunger, cyanosis, rapid pulse, and increased respiratory rate. Subcutaneous emphysema of the neck anteriorly and laterally was also palpable. Rebronchoscopy through the tracheotomy opening revealed no obstruction. X-ray, however, did show a massive bilateral pneumothorax and mediastinal emphysema. Both pleura were immediately tapped and 420 cu. c.c. of air withdrawn, following which 240 c.c. of air were withdrawn from a similar tap into the mediastinum. Water traps were connected bilaterally, but even with these measures, the patient expired four hours later. At autopsy a diagnosis was made of exudative tracheobronchitis, bilateral pneumothorax with mediastinal emphysema, and bronchopneumonia.

Tracheotomy is followed by complications much more frequently than a review of the literature shows. If there is no vio-

lation of technic in performing a tracheotomy, complications should be rare. The cases presented here, of mediastinal emphysema and pneumothorax, represent a complication which occurs more often than one is apt to believe. Neffson reports that 13.5 per cent of a series of cases with non-diphtheritic obstructive infections developed pneumothorax.

There are several possible causes for the development of these complications, such as direct injury to the pleura, or rupture of alveoli into interstitial pulmonary tissue with migration along the peribronchial and perivascular spaces to the mediastinum and eventual rupture into the pleural space. The most likely cause is excessive inspiratory movements with sucking of air into the mediastinum and eventual rupture into both pleural spaces. The usual explanation is that air enters the mediastinum through the wound in the cervical fascia, becomes imprisoned in the mediastinum, (especially when obstruction is not relieved), and finally reaches a tension high enough to rupture the mediastinal pleura, which is especially thin in children. When there is pneumothorax there always seems to be a coexisting mediastinal emphysema. Pneumothorax is usually bilateral. Jackson believes mediastinal emphysema is usually due to tight closure of the wound around the canula. Spontaneous pneumothorax has occurred from rupture of the visceral pleura in violent respiratory effort during impending asphyxia and is more likely to occur when previous adhesions exist.

The most frequent cause seems to be sucking of air through the tracheotomy wound into the mediastinum. Therefore, prevention of this is important, and can be accomplished by the observance of certain precautions, one of which is to eliminate the possibility of respiratory obstruction during operation. Avoid giving general anesthesia until the bronchoscope is in place, otherwise asphyxia may ensue inasmuch as the accessory respiratory muscles are put at rest and there is no voluntary stimulus. A bronchoscope in place before converts a gasping, restless, struggling child into a



quiet one, and the operation can proceed unhurried. It is well also to desist from opiates, too small an incision, or closing too tightly. Aspirate pathways frequently; however, postoperative obstructions may occur despite heroic measures. Another important precaution is to avoid the opening of avenues for air to get down. Anatomic dissection with demonstration and spreading wide of each distinct fascial layer, particularly pretracheal, should be avoided. Pretracheal fascia and cartilaginous rings should be cut at the same time and from below upward. Application of iodoform packs about the wound to seal off the spaces is considered very effective.

The time element, that is, when to perform the tracheotomy, has an important bearing on the success of the procedure. Michels believes that operation should be done as soon as adequate indications arise, not waiting for extreme conditions. Early diagnosis is essential inasmuch as time means so much, and is determined by the clinical picture, the physical signs, and the use of x-ray. The clinical picture may be so slight as to be unrecognized, with the patient rather free of symptoms, and yet, on the other hand, the patient may develop shock, cyanosis, and asphyxia in short order. The physical signs are generally severe dyspnea in which there is diminution in the volume and the force of the air through the tube. There is diminished excursion of the affected side with displacement of the heart to the opposite side. There is diminution of breath and voice sounds with hyperresonance and tympany. X-ray should be done as soon after tracheotomy as possible.

#### TREATMENT

When the symptoms are mild, careful watch should be exercised as air may be absorbed. When there is tension pneumothorax (air can get in but cannot get out) repeated decompression is necessary. Failure gives anoxia from massive venous stasis due to increased intrathoracic pres-

sure. Decompression should be done gradually without too great a shift in mediastinal pressure, or air embolism may occur. Decompression should be done with a special apparatus, or even with the pneumothorax machine and oxygen over the tube. Jackson suggests prompt bronchoscopic oxygen insufflation, constantly maintained until at least one lung has reexpanded.

Closed drainage of the chest may be necessary. Most observers feel that mediastinal surgery has met with only fair success and is to be avoided.

In unilateral pneumothorax, the mortality is usually less than 20 per cent as contrasted with bilateral pneumothorax in which the mortality is seldom less than 90 per cent.

Other complications, such as pneumonia and wound infections are usually treated with the sulfa drugs and penicillin. Frequently there are situations which arise and which appear to be pneumonias. These are actually areas of pneumonitis associated with atelectasis, in which the latter is due to plugs of mucus and similar concretions. Removal by the bronchoscope relieves this condition. Laryngeal and tracheal stenoses have been recently discussed and are usually due to high tracheotomy or misfit canula. As a means of preventing these it is well to cut below the second ring of trachea. The stenoses are associated with destruction of cartilaginous framework and may be corrected with core molds.

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## MYOCARDIAL ANEURYSM CAUSING ESOPHAGEAL OBSTRUCTION

### REPORT OF CASE PRESENTING A DOUBLE CARDIAC ANEURYSM WITH SEVERE DYS- PHAGIA NECESSITATING GASTROSTOMY

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Myocardial aneurysm involving the posterior wall of the left ventricle is not an uncommon finding secondary to myocardial infarction. Autopsy studies show involvement of this region in approximately 10 to 20 per cent of the cases in which ventricular aneurysm occurs.<sup>1, 2</sup> In about 10 per cent of all cases more than one aneurysm is found. Dysphagia, when present, is rarely a prominent symptom. The following case of double cardiac aneurysm with dysphagia and subsequent malnutrition severe enough to require gastrostomy is, therefore, considered worthy of note. A search through the literature fails to disclose a similar case. However, Strandell<sup>3</sup> describes an interesting case of aneurysm of the apex of the left ventricle, diagnosed, *in vitam*, in a luetic musician, aged 42. This patient complained of dysphagia characterized by a stinging pain in the lower chest four seconds after swallowing a mouthful of food. At autopsy, the discovery of a second aneurysm of the posterior wall of the left ventricle explained the patient's dysphagia for which there had earlier been no adequate explanation.

#### CASE REPORT

H. M., a 52-year-old, ambulant, colored male, veteran of World War I, was admitted to the Veterans Administration Hospital, Alexandria, La., on October 22, 1946, as a transfer from the U. S. Marine Hospital, Galveston, Texas, with symptoms of choking sensation in the suprasternal region, vomiting and soreness at the site of attachment of his gastrostomy tube to the abdominal wall.

He had no illness of consequence in childhood.

\*From the Medical Service of the Veterans Administration Hospital, Alexandria, La.

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His family history was non-contributory. Prior to his Army service he worked in several sawmills. He was married three times. In 1911, he contracted gonorrhea, which he treated himself with oral medication, and the following year he had a penile "haircut" which healed in a few days with applications of "bluestone" water. While in the Army he was found to have a positive blood Wasserman reaction for which he was given about thirty injections. In August 1918, he was hospitalized two weeks for complaints of headache, fever, malaise and generalized joint aching, and was diagnosed as having "tertiary" syphilis.

Following his discharge from the Army he worked in several logging camps as a "tong hooker" until 1939, then was employed as team driver, carpenter's helper and common laborer in an oil refinery, in shipyards and in lumber mills until December 1944. A blood Wasserman test in 1924 was negative. He drank "right smart" of whiskey, averaging about a quart weekly, from 1920 to 1935, but in the latter year he "quit drinking." His health prior to 1928 was fairly good except for occasional "rheumatism" pains in his knees and shoulders and "biliousness" which was usually relieved by purgatives.

In the early part of 1928, while he was engaged in loading logs, his tong slipped from the end of a log which was being hoisted, and he was jerked forwards. A few minutes later, he experienced a sharp, intermittent, non-radiating, tingling pain just below the cardiac apex. This pain, unlike anything he had ever experienced before, lasted for about ten to fifteen minutes, then gradually subsided. Despite the pain, however, he continued his work. He had no further trouble until two weeks later when the pain recurred, again lasting for several minutes. From then on, for the next six months, the pain recurred at shorter and shorter intervals, and its duration progressively increased until it would occur every few days and last for three to four hours at a time. Associated with this pain he noticed increasing dyspnea on exertion. These symptoms finally obliged him to give up his work and to enter the Charity Hospital in New Orleans. After a week's treatment with potassium iodide and corrosive sublimate, he began to improve symptomatically, and, in three weeks he was well enough to leave the hospital. Two weeks later he returned to his former occupation.

From 1928 to 1935, he experienced infrequent lower abdominal cramping pains after meals; these pains were usually relieved by soda, vinegar, or laxative tablets. In the early summer of 1935, while he was seated on the commode one afternoon, he felt "hot and faintified" and perspired profusely. He called for help and slumped backwards but did not lose consciousness. Following this incident he felt dizzy for an hour and stayed in bed for a few days. He then noticed increasing dyspnea on walking and working. In addition, his cramp-



ing abdominal pains recurred more frequently, on the average of once every two or three months, and would last a day or two before subsiding. He decided at this time to quit drinking alcohol. Nothing further of note occurred until the latter part of 1940, as he was talking to a mill owner in a lumber office, he suddenly lost consciousness and fell to the floor. When he recovered from this syncopal attack several minutes later, he felt dizzy and weak and had a mild headache. Following this episode, which was not attended either by paralysis or convulsions, he stayed in bed for a few weeks.

In the spring of 1942, following a routine blood serological test at a Health Clinic, he was told that he needed "shots" for his blood. He was given weekly intravenous and intramuscular injections for a period of five months and, at the end of this time, had a negative Wassermann. In July 1944, his cramping lower abdominal pains became so severe that he visited several physicians for relief. X-ray studies were made, revealing an ulcerated stomach, and he was admitted to the City Hospital in San Francisco for treatment. Under Sippy regime, his pains gradually subsided and, after about a week, he was discharged from the hospital. Within a few days, he returned to his work. On September 27, 1944, as he was stacking lumber, he suddenly felt excruciating pain to the right of his umbilicus and had a sensation of extreme weakness. He was readmitted to the City Hospital, where he was immediately operated upon and found to have a perforated ulcer. His post-operative course was uneventful; the lower abdominal pains, which had been bothering him since 1935, disappeared, and, after fifteen or sixteen days, he felt well enough to leave the hospital. Six weeks later, he returned to work in a sawmill. He worked until December 21, 1944, when he slipped while climbing a stack of lumber and injured his back.

In July 1945, he had almost completely recovered from his injury when he experienced a siege of hiccoughs and vomiting which lasted continuously for a week. For a few days prior to this episode, he felt "droopy and weak," and "couldn't stand to walk much." One evening, towards 11:00 P. M., he awoke feeling "sick in the stomach," then commenced to vomit and to hiccough. His vomitus consisted at first of food, then of a slimy yellowish liquid. He was unable to retain even liquids. After a week's vomiting and hiccoughing, he had a respite for a day or two; then the symptoms recurred. There was very little nausea associated with his vomiting. He began to lose considerable weight as a result of his vomiting, and sought hospitalization.

During September, and again during October, 1945, he was treated at the U. S. Marine Hospital, Galveston for duodenal ulcer, with little relief of his symptoms. He was readmitted on December

17, 1945, when an electrocardiogram was made, showing evidence of an old posterior wall infarction. Diagnoses of duodenal ulcer and aneurysm of the left ventricle due to infarction were then made. Under treatment with Sippy and liquid regime, the patient showed some symptomatic improvement but was never entirely free of his choking sensation or vomiting. Ten days after his discharge from the hospital on March 2, 1946, he had to be readmitted. His weight by this time had dropped to 114 pounds as compared with his normal weight of 165 pounds at the onset of his illness in July 1945. Gastric analysis showed a free HCl of 118 degrees. Fluoroscopic study and a gastro-intestinal series disclosed a practically complete esophageal obstruction behind the heart shadow, with barium unable to pass beyond this point. A calcified shadow was noted in the region of the left ventricle. The roentgenologist's impression was carcinoma of the esophagus. In view of the patient's marked emaciation, a gastrostomy tube was inserted for feeding purposes on April 12. The patient was now able to retain part of his nourishment. Barium study of the esophagus was repeated on June 27; it now revealed an incomplete obstruction. There was a persistent, smooth, symmetrical constriction of the esophagus "posterior to the portion of the cardiac silhouette formed by the right auricle," with delay of barium at this point. The previous impression of stricture on a carcinoma basis was now considered doubtful.

In July 1946, the patient was given a week's furlough during which time he adhered to a soft diet but took no gastrostomy feedings. Although he still had some vomiting while at home, his general condition remained essentially unchanged. Upon his return to the hospital, it was felt that his tube could be removed, and, accordingly, on the 25th of July the gastrostomy tube was removed and the opening closed. The patient appeared to be getting along fairly well when, on August 1st, after eating a few mouthfuls of roast meat, he had recurrence of his vomiting. On August 5th, his present gastrostomy tube was inserted. On August 15th, esophagoscopy was performed, and a portion of tissue was removed for biopsy. No tissue suggestive of carcinoma or other malignancy was found. At the esophageal-gastric junction, the mucosa appeared granular. A diagnosis of cardiospasm was then made. A repeat fluoroscopic study on August 22nd disclosed that the calcified mass overlying the cardiac silhouette in the lower portion of the left chest was not attached to the diaphragm and showed no pulsations, either intrinsic or transmitted. The roentgenological impression was benign mass, lying either within the pericardial fat or in the portion of the lung anterior to the pericardium.

In the latter part of August, patient was sitting in a wheel chair when he suddenly began to feel

"dizzy and hot," and "passed out." When he regained consciousness several minutes later, he felt weak and dizzy; these symptoms persisted for several hours. Injections of novocaine into the dorsal sympathetic chain were considered for relief of his cardiospasm, but he repeatedly refused to have these performed because of his weakness. He was then transferred to the Veterans Administration Hospital in Alexandria, La., for domiciliary care.

Examination on admission revealed a chronically ill-appearing, ambulant colored male, height 6' 2", weight 125 pounds, who had an indwelling gastrostomy tube. His chief complaints were occasional choking sensation in the suprasternal region, vomiting, and soreness at the site of insertion of his gastrostomy tube. His vomiting bore no fixed relation to his meals; it would occur at any time of day or night. He described its onset as follows: "A choking comes on me (pointing to suprasternal notch) and cuts my wind off. Seems like if I can belch, it gives me all the relief. Otherwise, I have to vomit." His vomiting rarely exceeded two mouthfuls of a slimy fluid, which was occasionally mixed with food. There was little nausea, and no burning or bitter sensation, associated with his vomiting. His vomitus never showed any blood. After a vomiting spell, he would stay as quiet as possible for two or three hours, at the end of which time he would generally "catch his breath" better.

He appeared somewhat pallid, but was not dyspneic at rest. His thorax was long and slightly emaciated. The point of maximum impulse was visible and palpable in the 6th intercostal space,  $\frac{1}{2}$  cm. lateral to the left nipple. Upon palpation, a definite expansile impulse was felt at the apex. Contrasting with this finding, the first heart sound was faint over all cardiac areas. The second apical sound was clicking in character.  $A_2$  was louder than  $P_2$ . The heart rhythm was regular, except for the presence of occasional extrasystoles. No thrill was palpable. A soft, blowing, non-radiating, late systolic murmur was heard at the apex and at the aortic area. Upon moderate pressure with the bell-type stethoscope in the region of the apex, with the patient in the upright position, a short scratching sound was heard during late systole. This sound was inconstant, however, and disappeared when patient was in the supine position. The pulses were equal and synchronous. There was no undue peripheral arteriosclerosis. The pulse rate was 78 per minute. Blood pressure readings in both arms were 114/84. The lungs were negative. Other physical findings were essentially negative.

X-ray of the chest in the PA view (Fig. 1) revealed a cardio-thoracic ratio of 53 per cent, and an ovoid area with calcified border measuring approximately 5.5 cm. by 4.5 cm. near the apex of the heart. On fluoroscopic examination, an expansile pulsation was visible on the posterior

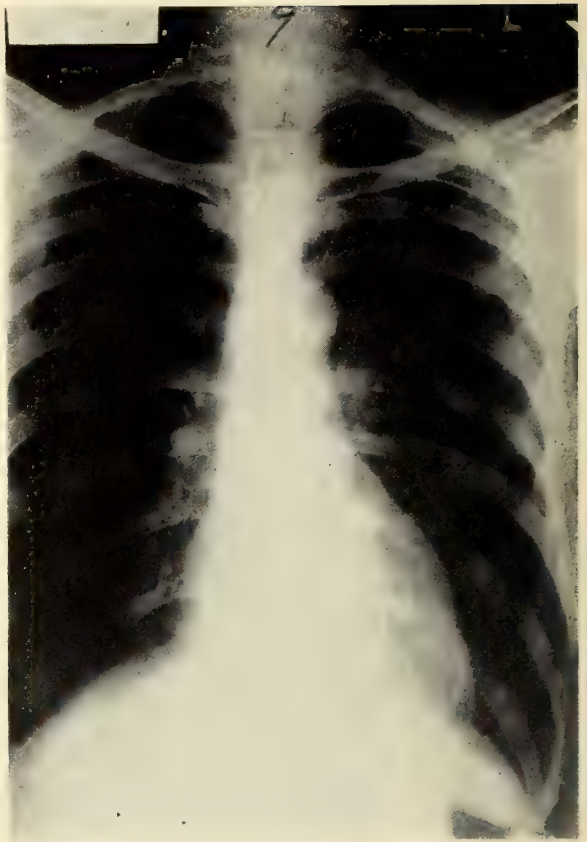


Figure 1. PA view of chest showing aneurysm with intramural calcification at the apex of the left ventricle.

aspect of the heart. The esophagus was found to be constricted in its distal third; this constriction was apparently due to pressure from an aneurysm of the posterior portion of the heart. Above the point of constriction, the esophagus appeared slightly dilated (Fig. 2). No defects, tenderness, or niche formation were noted in the stomach or duodenal cap. The stomach was entirely empty at the end of one hour. The gastrostomy tube was located in the distal third of the lesser curvature. An electrocardiogram made on admission showed evidence of an old posterior wall infarction, with coronary-type inversion of  $T_2$  and  $T_3$ , a  $Q_2T_2$  and  $Q_3T_3$  pattern, and occasional premature ventricular contractions (Fig. 3). The blood Wassermann and Kahn were negative. The blood count on admission showed a hypochromic anemia, with an erythrocyte count of 3,860,000 and a hemoglobin of 54 per cent.

Patient was given a transfusion of 250 cc. citrated blood on November 4th. He was placed on a soft diet and fed, in addition, per gastrostomy tube, 150 cc. tid of a 1000 calorie formula consisting of milk, sugar, tomato juice, whole eggs and brewer's yeast. Medication consisted of tincture of bella-





Figure 2. Left anterior oblique view showing dilatation of esophagus above area of constriction resulting from aneurysm of the posterior wall of the left ventricle. Note intramural calcification at apex of left ventricle.

donna, 10 drops tid, and nitroglycerin tablets, gr. 1/100, sublingually, prn.

Under this treatment, he showed definite symptomatic improvement. His weight increased to 137 pounds. Gastric analysis of a fasting specimen showed a free HCl of 40 degrees and a total acidity of 78 degrees. His appetite was good. Although there was a marked lessening of the discomfort resulting from his choking sensation, he still experienced, once or twice a week, some choking on swallowing; this was relieved by his vomiting. The nitroglycerin sublingually appeared to be of definite value in diminishing his choking sensation. Early in December his tube feedings were discontinued for a period of two weeks. During this time his weight remained stationary. In the latter part of December, he had another syncopal episode; while sitting near his bedside he suddenly felt "weak, dizzified, and blind", then the next thing he remembered was finding himself in bed. At the Christmas holidays he was given a two weeks' furlough, during which time he supplemented his oral feedings with sweetened milk through his

gastrostomy tube. Upon his return to the hospital, his general condition was satisfactory. At the present time, he is freely ambulant, but experiences slight dyspnea when he walks from his ward to the gate, a distance of approximately half a mile.

#### COMMENT

This case presents several unusual features. The patient's history and his symptoms of recurrent precordial pain, increasing in intensity and duration over a period of several months, strongly suggests that he had an initial coronary occlusion in 1928. Despite his pain, he continued his arduous work. The added strain thus imposed upon a weakened myocardium, it is reasonable to suppose, resulted in the formation of an aneurysm at the apex of the left ventricle, the most frequent site for such a lesion. Fulton<sup>4</sup> has called attention to the significance of recurrent, prolonged pain follow-

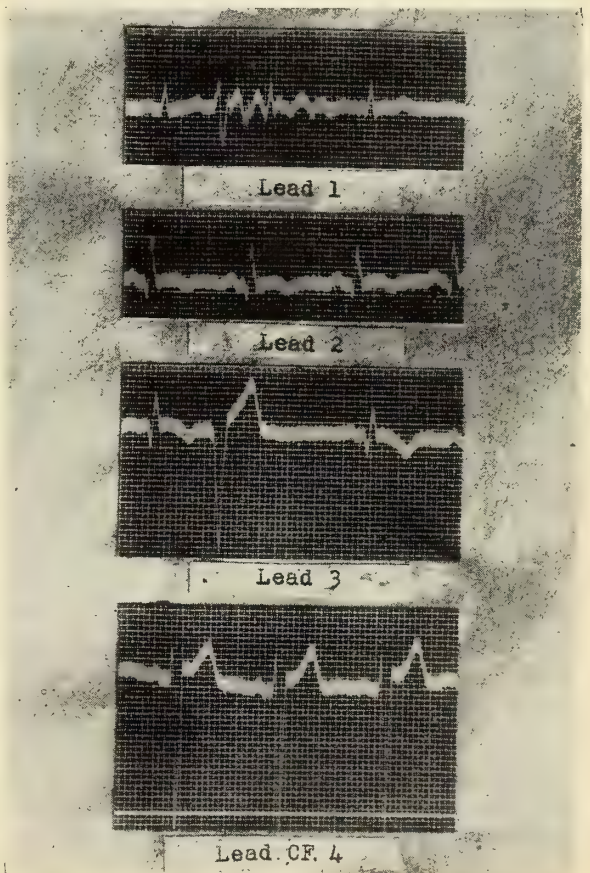


Figure 3. Electrocardiogram taken 10-23-46 showing evidence of old posterior infarction and occasional premature contractions, one of which is interpolated.

ing the initial episode in the diagnosis of cardiac aneurysm, and has stressed the importance of insufficient rest following myocardial infarction in its causation. Evidence of this initial aneurysm is now furnished by the ovoid mass with intramural calcification at the apex. The absence of pulsation is explained by the intramural thrombus formation and calcium deposit.

A second aneurysm then occurred, probably in July 1945, this time involving the posterior wall of the left ventricle and causing a marked constriction of the lower third of the esophagus. Considering the more or less sudden onset of this patient's dysphagia, the evolution of this aneurysm must have been rapid. Evidence of this second aneurysm is obtained from fluoroscopic study, which reveals an expansile pulsation on the posterior aspect of the heart, and from the electrocardiogram, which shows evidence of an old posterior wall infarction.

Since esophageal obstruction due to aneurysm of the posterior wall of the left ventricle is such a rare entity, it is not surprising that carcinoma of the esophagus was at first suspected as the etiological factor. Further studies, however, cast doubt upon this diagnosis. A diagnosis of achalasia was then made. The significance of the calcified mass in the apical region was overlooked. It was thought to be a benign tumor, lying either within the pericardial fat or in the lung tissue anterior to the pericardium. Some significance should be attached to this patient's syncopal episodes, the first two occurring before, and the second two subsequent to, his perforated ulcer. Among the causative factors to be considered are minute cerebral emboli arising from an aneurysmal mural thrombus, cerebral anemia secondary to paroxysmal cardiac arrhythmia, cerebral arteriosclerosis and, possibly, luetic cerebral endarteritis.

In the association of syphilis with double cardiac aneurysm this case bears a striking resemblance to the case described by Strandell. Another feature of interest is the patient's state of relative well-being at

the present time. If, as appears likely, his initial myocardial infarction and aneurysm occurred in 1928, then he was able, nevertheless, to engage subsequently in arduous activities for a period of sixteen years. Although mild esophageal obstruction has been noted occasionally in cases of aneurysm of the posterior wall of the left ventricle<sup>3, 5</sup>, it is very unusual for the dysphagia to be so prominent a symptom as to require gastrostomy.

#### SUMMARY

1. An unusual case of double cardiac aneurysm in a 52-year-old colored male is reported, with a predominating symptom of dysphagia of such severity as to require gastrostomy for feeding purposes. The first aneurysm probably occurred in 1928, as a sequela to coronary occlusion, and is now recognizable by a calcified, ovoid, non-pulsating mass at the apex of the left ventricle, the most common site for cardiac aneurysm. A second aneurysm then developed, probably in July 1945, this time involving the posterior wall of the left ventricle, and causing a marked constriction of the lower third of the esophagus. This aneurysm is demonstrable by fluoroscopy and its etiology is confirmed by the electrocardiogram, which reveals evidence of an old posterior wall infarction.

2. Relative well-being and an active life are not incompatible with aneurysm of the heart. In the present case, the patient engaged in the arduous labor of a logger and team driver for a period of sixteen years following the occurrence of his initial aneurysm.

3. Pressure upon the esophagus from a cardiac aneurysm, although rare, should be considered in the differential diagnosis of dysphagia. In the present instance, the patient's symptoms were at first attributed to carcinoma of the esophagus, then to achalasia.

The author is indebted to Dr. Oza J. LaBarge, Chief of the Medical Service, and to Drs. Arthur G. Sullivan, Allen C. Winters, and Samuel A. Shelburne for their interest and helpful criticisms.

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—O—

## PAPILLOMA OF THE GALLBLADDER: CASE REPORT

GORDON MCHARDY, M. D.

AND

EDWIN EDWARDS, M. D.

NEW ORLEANS

The relative rarity of cholecystic papilloma has been previously presented by one of us.<sup>1</sup> Kirklin's<sup>2</sup> diagnostic roentgen accomplishments are recognized. A single case study<sup>3</sup> since ours likewise was diagnosed roentgenologically and comments were made of the possible, but unlikely, relationship to carcinoma of the gallbladder. We take issue with Greenwald's disregard for malignant potentiality on the basis of prevalence of calculosis with carcinoma of the gallbladder, while rarely are papillomas associated with calculi. Generally, while the frequent association is recognized it is conceded that the presence of calculi is merely incidental to the diagnosis of cholecystic malignancy; one could not on this basis discount malignant potentiality of a gallbladder papilloma. Phillips<sup>4</sup> reports calculi complicating his reported cases of papilloma.

An important point emphasized by Greenwald<sup>3</sup> that these lesions are overlooked at operation because of the impression of a normal gallbladder grossly on appearance and palpation, was further illustrated in our case in which the surgeon was reluctant to remove the gallbladder. Further, the pathology department initially missed the papilloma, as it had twisted from its pedicle and lay free in the lumen of the gallbladder.

### CASE REPORT

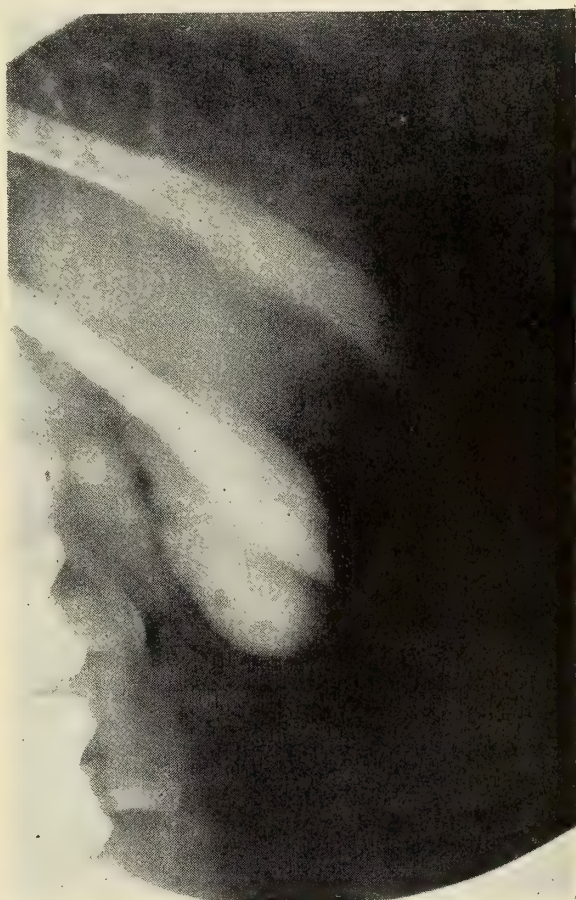
Mrs. L. M. E., a fifty-one year old obese white female was admitted to the gastrointestinal clinic complaining of postprandial epigastric fullness of five months' duration, accentuated by fatty and fried foods, and at infrequent intervals characterized by typical episodes of biliary colic with nausea and emesis.

From the Department of Medicine, Tulane University School of Medicine and the Gastrointestinal Clinic of Touro Infirmary, New Orleans, La.

Physical examination, during an episode of acute manifestation, revealed only right upper abdominal tenderness and muscle splinting.

There were no contributory laboratory findings.

The roentgen findings repeatedly confirmed the presence of a constantly located, marginal, radio-lucent shadow as illustrated which was assumed to be a papilloma.



Cholecystectomy was performed by Dr. Irving M. Essrig. Exploration revealed no gross cholecystic disease and cholecystectomy was only performed upon insistence.

The pathologist reported: Benign Glandular Polyp of the Gallbladder.

### CONCLUSION

Rarity, roentgen diagnosis, separation of the polyp from the pedicle, obvious potentialities, and the simulation of symptomatology to biliary colic stimulate us to publication of this case.

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## REPAIR OF PAROTID DUCT FISTULA

WITH ONE CASE REPORT

LEONARD H. STANDER, M. D.

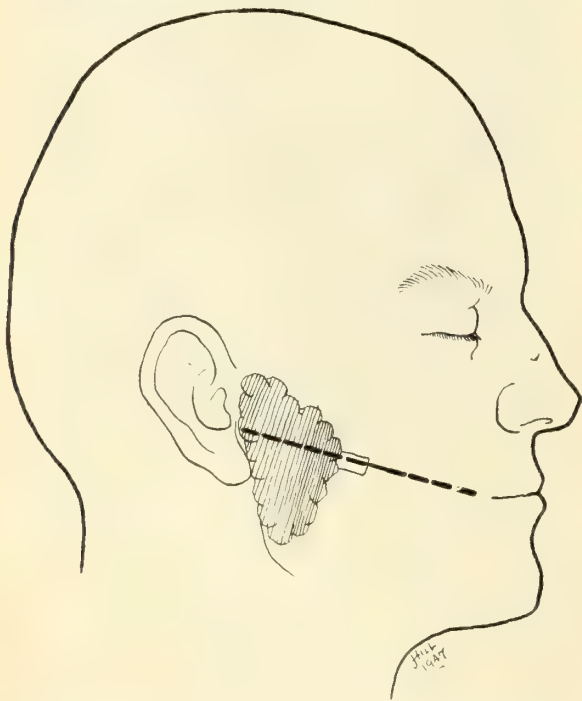
BATON ROUGE

AND

CLAUDE C. CRAIGHEAD, M. D.†

NEW ORLEANS

The parotid duct, also known as Stensen's or Steno's duct, is approximately five centimeters in length and lies one finger's breadth below the zygomatic arch. It emerges from the extreme anterior portion of the gland and runs forward obliquely on the masseter muscle to the mucous membrane of the cheek. The course of the duct on the masseter muscle is represented by a line drawn from the lower margin of the concha of the ear to the commissure of the lips. The duct opens into the mouth opposite the second upper molar tooth.



The repair of division of the parotid duct may be considered from the standpoint of injuries which are recognized at the time of occurrence and those which are not detected until later. The results are uniformly good in acute injuries with primary repair. However, when injury to the parotid is not

detected at initial examination and followed by suturing of the laceration in that region, the repair becomes more difficult.

In primary repair the severed duct can be anastomosed, end to end, after the introduction of some type of inlying dowel which is brought through the oral orifice and fixed to the buccal membrane by a single suture. The dowel should be left in place approximately three weeks. One strand of catgut or silkworm gut is considered satisfactory to keep the duct open. The suture line should not include the mucous membrane of the duct as this predisposes infection.

The most difficult problem encountered is that of a patient with a persistent salivary fistula draining through the scar on the cheek. It is a well recognized fact that an abnormal opening usually closes if the normal channel has an adequate pathway.

Various modifications of von Laugenbeck's<sup>1</sup> technic have been used successfully for secondary repair. Braun<sup>1</sup> employs a mucous membrane tube, Smith a split thickness of skin over a glass rod to reestablish an epithelial lined tract. Glascock<sup>2</sup> threads a piece of silkworm gut through each end of the duct, carries the gut through the gland and attaches a small shot on either end of the suture—one at its exit through the skin, another at its emergence from the mucous membrane.

For many years surgeons have used what is known as a "Seton" suture<sup>3</sup> to produce an internal fistula proximal to severance of the duct. This is accomplished by passing one non-absorbable suture around the duct from within the buccal cavity, tying the suture loosely, and each day pulling the suture slightly until it works through, thereby producing an internal fistula which influences the external fistula to close. However, in this method of treatment the duct papilla with its valve-like action is lost. Newman and Seabrook<sup>4</sup> state that it is essential that the papilla be preserved because of its protective action, its presence being a bar to ascending infection.

If there is any evidence of inflammation present in the cheek laceration it is com-

†From the Charity Hospital of Louisiana, New Orleans, La.



pletely reduced by the use of local heat and penicillin before the institution of operative procedures. The anastomosed ends of the duct have a much better chance of primary union if the wound is clean. Preoperatively a small probe is introduced daily into the buccal opening of Stensen's duct for the purpose of keeping the distal portion of the severed duct dilated thereby enhancing the possibilities of its postoperative function. There must be no stricture of the distal end of the duct if the fistula is to remain closed after operative treatment. The patency of the proximal and distal ends of the duct can be readily ascertained by lipoidal sialography.<sup>5</sup>

Endotracheal intubation is the anesthesia of choice. Local analgesia is contraindicated because the fistulous tract is a potentially infected area. Initially the old scar is completely excised and the severed ends of the parotid duct are dissected free. A ureteral catheter is passed through the distal end of the duct and brought out through the buccal orifice; the other end is threaded into the proximal end of the duct. The proximal and distal ends of the duct are then anastomosed over the catheter using fine interrupted sutures which are passed through the fascial layer of the duct. On the operative side, the catheter is fixed to the commissure of the lip with a single suture and the excess catheter is clipped off. Interrupted sutures are used for closure of the platysma and skin and a pressure dressing is applied.

Penicillin is recommended postoperatively but it is not considered necessary. The catheter is left in position for three weeks. The patient is put on a regular diet, supplemented by pilocarpine and ammonium chloride, to stimulate a free flow of parotid secretion. The small opening in the catheter is kept patent to facilitate drainage. In the event of plugging the catheter is gently twisted. It is our opinion that drainage through the lumen of the catheter accounts for the success of this procedure. This contention, however, is disputed in the literature wherein it is stated that the lumen of the catheter is not essential and

further that it does not provide a real channel.<sup>6</sup>

#### CASE REPORT

E. P., a colored male, aged 33, at the time of admission had the chief complaint of swelling of the right side of the face.

Two weeks prior to examination the patient sustained a cut on the right side of the face inflicted with a pocket knife. An hour later the skin laceration was sutured by his physician. Five days later the sutures were removed and he began to eat solid food again. The right side of his jaw commenced to swell. He returned to his doctor who prescribed sulfa tablets and "rest pills." The patient soon learned that if he "picked the scab off" the wound on his right cheek clear yellow fluid would drain, the swelling would subside, and the pain would disappear. However, as soon as he began to eat again, the mass recurred.

Physical examination revealed a swelling of the right side of the face in the region of the parotid gland. A scar extended from just below the concha of the right ear forward onto the hollow of the cheek. There was a small area on the anterior portion of the scar covered by an encrustation which, when removed, allowed clear yellow fluid to escape.

The patient was operated upon under endotracheal anesthesia. The severed ends of the parotid duct were dissected free and anastomosed over a ureteral catheter which was brought out through the oral orifice of the duct, and fixed to the commissure of the lip with a single suture. The wound was closed in layers, using fine interrupted non-absorbable sutures. A pressure dressing was applied.

The patient was allowed to eat the first postoperative day. The ureteral catheter was left in place for three weeks. A good functional result was obtained.

The patient was last seen six months postoperatively. At that time he stated that he had experienced no swelling of the jaw following his operation.

#### SUMMARY

1. A better functional result of the parotid duct is achieved when it is repaired at the time of injury.
2. If the duct is not repaired at the time of original injury, no repair should be attempted until the laceration of the cheek is well healed.
3. Preoperatively the duct should be kept open by daily probing, and postoperatively by some type of inlying dowel, preferably a ureteral catheter.
4. A good functional result is more difficult to attain once a fistula has developed.
5. A typical case is reported.

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## NEW ORLEANS

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## FEDERAL SUBSIDY OF PEDIATRIC EDUCATION

Federal subsidy of medical education increases the risk of state medicine.

A recent action by the Executive Board of the American Academy of Pediatrics gives organized medicine some cause for concern.

On February 8, 1948, the Executive Board of the American Academy of Pediatrics accepted a report from its committee for the improvement of child health. The sense of this report was somewhat to the following effect: That there were not enough well trained doctors in America to

care for the child population. Inference is made that the majority of doctors caring for children are not competent to do so because they have not had hospital training in pediatrics. It is also stated that the doctors are poorly distributed; and further, that the usual channels of pediatric education do not have sufficient money to properly train all the pediatricians needed to take care of America's children. To meet what is described as an urgent situation, this report calls for Federal subsidy of pediatric education. This is to be accomplished by means of grants in aid to medical schools. Congress is being asked for five million dollars to be administered by the Federal Security Administration in direct support of pediatric education. This money is to be used in various ways, such as scholarships or fellowships, or expenses for the staff of pediatric departments when visiting affiliated or outlying hospitals for teaching ward rounds, support for maintaining high standards of pediatric education, and other purposes directly related to pediatric education.

In keeping with such a plan, the Bill was introduced by Senator Thomas of Utah on April 30, 1948. It became Senate Bill No. 2588. Interested parties have appeared in support of this Bill.

Although these plans which are indicated above have passed the Executive Board of the American Academy of Pediatrics, it does not appear, so far, that the Academy as a whole has accepted them. On the contrary, there are some indications that many pediatricians feel that this would be quite inimical to the interests of organized medicine.

This plan of Federal subsidy of pediatrics, if allowed to operate even a few years, would in effect be pediatric State Medicine. If State Medicine is introduced insidiously in this fashion, the difficulty in fighting it in the other fields of medicine is only too obvious. As has been pointed out here before, one has only to look at the extraordinary growth of power of bureaucracy in regard to income taxes to realize how completely dominant so small a thing as a Gov-

ernmental bureau can become in the lives of the entire nation.

Recent rulings of the Supreme Court of the United States indicate that it is the present trend to require participation by negroes in all phases of State and Federal educational policy. The effect of adherence to such provisions in the South would, in many respects, add a great embarrassment even to the problem of State Medicine in the South.

Accordingly, those who support the policies and interests of organized medicine are urged to utilize their influence in opposition to Senate Bill No. 2588 and prevent, if possible, the suckling infant of socialized medicine being wheeled into our midst in a baby carriage.

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#### TREATMENT OF HYPERTENSION WITH RICE DIET

In 1944, Kempner presented a rice diet for hypertension. The diet contains in 2000 calories not more than 5 grams of fat, and 20 grams of protein, which is derived from rice and fruit, and not more than 200 mgs. of chloride, and 150 mgm. of sodium. The patient takes an average of 250 to 350 grams of rice a day. No sodium chloride or milk is added. If sodium concentration of plain water is greater than 20 milligrams per liter, distilled water should be used. All fruits and fruit juices are used, but not nuts, dates, and avocados; not more than one banana a day; white sugar may be used as desired. Tomato and vegetable juices are not allowed. Supplementary vitamins are added to the diet in the usual form.

The author advocated the rice diet in all serious instances of acute and chronic nephritis and in hypertensive disease. The subjective state of the patients on the rice diet was reported as much improved. Objective findings are as follows: Five hundred patients were on the rice diet for a period of four days to eight hundred and ninety-eight days. The diet was ineffective in 178, including 26 who died. In 322 of the 500 patients, the diet was beneficial, that is, its use was followed by either a reduction in mean arterial blood pressure

of at least 20 millimeters, or a reduction of heart size with a change in the transverse diameter of 18 per cent or more, a change in T-1 from a complete inversion to upright, or disappearance of severe retinopathy.

Dick and Schwartz, from the Department of Medicine of the University of Chicago, tested the effect of the rice diet on experimental hypertension in dogs. In this experiment, at the end of eight weeks on the diet, the average arterial blood pressure of the 12 dogs had fallen from 181.6 mm. of mercury to 138 mm. of mercury. In certain dogs, the reduction was as much as 88 per cent. All dogs lost weight on the rice diet, the average being 20 per cent. Grollman and his associates studied the effect of the rice diet with a view to determining the possible value of the absence of sodium in the diet. For this purpose, 100 patients with essential hypertension were placed on a diet, adequate in other respects, but lacking in sodium. Periods of observation varied from several weeks to twelve months. There was a lowering of blood pressure to approximately 155/95 in 20 per cent, and a lowering of the diastolic pressure to, or below, 95 in an additional 15 per cent.

Impression gained from consideration of these several investigations is that dietary treatment of hypertension needs further study. While some of its effects may be due to lack, or sharp reduction in the total amount of sodium consumed, certain other benefits appear to be due to the rice and the fruit. A diet as rigid as Kempner has outlined is one which would be very difficult for the majority of hypertensive patients. On the other hand, when complications of a certain grade of severity appear, the interest of the patient in maintaining the diet will be in proportion to the severity of those complications. It is suggested in a certain portion of these studies that a metabolism of nitrogen and salt is different on the rice diet from what it would be expected to be on a purely fasting diet.

A new field of speculation and interest in hypertension has thus been opened.



## ORGANIZATION SECTION

**The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.**

***An informed profession should be a wise one.***

### NATIONAL HEALTH ASSEMBLY

WASHINGTON, D. C.

MAY 1-4, 1948

The Secretary-Treasurer of the Louisiana State Medical Society was appointed by the President of the Society to attend this conference as a representative of the organization. Efforts were made to secure a formal delegate's invitation, by writing to Oscar Ewing, Administrator of the Federal Security Administration, however this was unsuccessful and a reply to the request sent to Mr. Ewing was not received. After arriving in Washington every effort possible was made to secure a delegate's invitation to no avail. A reporter's pass was secured and the State Society was thereby represented by the Secretary-Treasurer as a reporter for the New Orleans Medical and Surgical Journal. This proved to be very serviceable as it afforded the privilege of going from one panel meeting to another without interference. The delegates were assigned to one special panel and were unable to get this changed unless request was made for such a change. This press card also served another useful purpose in making available copies of addresses made before all sessions and final reports and recommendations and various other available releases. All of this material has been assembled in book form and is in the office of the Society for ready reference.

On the whole it is felt that the meeting was a successful one especially due to the fact that the 80 doctors in attendance as delegates were able to keep out of the reports the adoption of compulsory health insurance. It was common belief that this conference had been called for the purpose of endorsing this form of national insurance.

The voluntary prepayment plans became more understandable to the public in the

manner in which they were presented and discussed. It is believed that the societies sponsoring these voluntary plans gained a lot of friends and supporters as a result of the manner in which they conducted their presentations.

Outstanding in the reports from most of the panels emphasized the fact that the federal government in subsidizing or advancing money for any federal purpose in any state should require that such money be spent on such projects without segregation and no discrimination on account of race, color, creed or religion.

The whole meeting seemed to be packed with a designated, specific purpose, namely, for endorsing federalization of medicine. There were assembled some eight or nine hundred individuals; a very cosmopolitan group composed of scientists, doctors, researchers, labor people, welfare workers and most important of all, most of those people were from the federal government and principally from the Federal Security Administration. They seemed to have priority of receipt of invitations. Some of the speakers who represented labor and other groups could hardly speak English. The renowned Dr. Mike Davis made a statement that "the more the AMA opposes federal health insurance the more surely will the country be driven into state medicine".

Throughout the meeting in the section on medical care, it was quite common to see lobbying by various types of people, moving around amongst the audience prompting and conversing quietly with their followers, evidently preparing some strategic action on their part. The audience in the medical care section at times broke away from what would ordinarily be considered good decorum for such a gathering. For example when a favored speaker would make a point in his discussion which they approved they would clap and holler and cheer and when

the opposition spoke and made some remark with which they did not agree they did not hesitate to boo. Sometimes it was felt that if one walked into a communistic meeting or a labor union gathering the set-up in this regard could not have been more idealistic.

One of the most outstanding observations on the part of the representative of the State Society was that with all of this the representatives of the medical profession did not lose their heads and were complimented several times on the manner in which they conducted their work and presented their cause.

Following is further information concerning this Assembly, as reported by Dr. Jos. S. Lawrence, Director of the Council on Medical Service of the American Medical Association.

"The National Health Assembly began its sessions on Saturday morning, May 1st, with more than eight hundred delegates registered of whom approximately one-fourth were physicians, the others being members of State Health Departments, social workers, representatives of labor unions, farm groups, consumers, and civilian organizations. At the opening session the delegates were welcomed by Honorable Oscar R. Ewing, Federal Security Administrator; and Howard M. Kline, the Executive Secretary, announced that the delegates would be registered into fourteen divisions, each with its own room, and most of them located in the Statler Hotel where the headquarters of the Assembly were established.

The machinery of the Assembly consisted of an Executive Committee appointed by the Administrator more than a month ago and a chairman and steering committee for each division. The Executive Committee advised the Administrator on the details of the general program and, at the close of the Assembly, will consider with him the reports submitted by the division chairmen. The steering committees of the divisions prepared in advance statements suggesting subjects for discussion by the members of the division. At the opening meetings of

the divisions, these statements were read or delivered, after which open discussion was entertained."

Membership in the divisions ranged from seventy-five upward, the largest division being that of "Medical Care" in which several hundred were registered. A list of the sections follows:

1. What is the Nation's Need for Health and Medical Personnel?
2. What is the Nation's Need for Hospital Facilities, Health Centers and Diagnostic Clinics?
3. What is the Nation's Need for Local Health Units?
4. Chronic Disease and the Aging Process.
5. A National Program for Maternal and Child Health.
6. A National Program for Rural Health.
7. What is the Nation's Need for Research in the Service of Health?
8. What is the Nation's Need for Medical Care?
9. State and Community Planning for Health.
10. Physical Medicine and Rehabilitation.
11. What Can Be Done to Improve Dental Health?
12. A National Program for Mental Health.
13. What Can Be Done to Improve Nutrition?
14. A National Program of Environmental Sanitation.

"The divisions were in session Saturday afternoon, Sunday morning and afternoon, and Monday afternoon. Several general sessions were held which were open to the public. On Saturday evening there was a dinner for the delegates and their friends which was addressed by President Truman. There were also two special luncheons.

The findings of the various divisions will be published in time. The recommendations and reports of the committees of the division were not voted upon by the members of the committees. No efforts were made in any division to record opinion on any matter that was under discussion. I was



not registered as a delegate to any division, but with the assistance of a press card I was able to visit all the divisions while they were in action. The general opinion is that the committees took their work very seriously. Two objectives seemed to present themselves in one form or another to each group: (1) that the problem assigned to it is a community problem and (2) that its solution is the responsibility of all of the agencies of the community.

In the most instances, of course, the subject under discussion related to health, but the delegates recognized that the problem could not be solved by physicians and health authorities alone. *In only two or three instances did the committees emphasize the need of Federal assistance.* Even in the Medical Care Committee compulsory health insurance gave way to consideration of voluntary plans as is evidenced by a statement which was submitted by the Steering Committee of the Medical Care Division at its last session.

There was much discussion as to how the prepayment plans should originate and by whom they should be controlled. Representatives of the cooperatives, the consumers, and the unions generally felt that control should not be left to the physicians alone, and opposition was expressed to legislation extant in more than twenty states requiring that no plans be organized without approval of the State Medical Association.

At a general session on Tuesday morning, Quincy Howe, of the Columbia Broadcasting System, reported the findings of all of the divisions and commented that this is probably the first such occasion where laymen and physicians worked together so zealously to develop a health program. All divisions *approached their tasks from the community rather than the national level.* The Assembly closed with a luncheon held in observance of the 150th Anniversary of the U. S. Public Health Service."

## LOUISIANA STATE MEDICAL SOCIETY NEWS

### CALENDAR

#### PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

#### SABINE PARISH MEDICAL SOCIETY

The meeting date of the Sabine Parish Medical Society will be the second Wednesday of each month, and the place will be rotated from Zwolle, to Many, to Pleasant Hill, to Converse. The next meeting will be in Zwolle on June 9 at the home of Dr. L. H. Murdock.

#### CARDIOLOGY COURSE IN MEXICO CITY

This note under College News appeared in the Annals of Internal Medicine, April 1948, p. 877.

This will be of great interest to Louisiana physicians who are planning to take post graduate

work and a vacation in a cool climate at the same time.

A two-week course in cardiology August 2 to 13 will be held at the National Institute of Cardiology in Mexico City under the direction of Dr. Ignacio Chaves, F. A. C. P., with the instructional staff being made up of a number of outstanding Mexican teachers who speak English, supplemented by several distinguished guest teachers from the U. S. Sessions will be held in the mornings daily, with the afternoons free for entertainment, sight-seeing and visits to other institutions. This course presents an opportunity for a most enjoy-

able two weeks' vacation, partly devoted to study and observation of methods in our neighboring Republic. Wives and members of the physicians' families are invited, and adequate hotel accommodations will be available. Those interested in this course are requested to communicate at once with the Executive Secretary of the College, Mr. E. R. Loveland, 4200 Pine Street, Philadelphia 4, Pennsylvania, so that some definite estimate can be prepared for the Director and the hotels.

#### THE AMERICAN CONGRESS OF PHYSICAL MEDICINE

Will hold its twenty-sixth annual scientific and clinical session Sept. 7, 8, 9, 10 and 11 inclusive, at the Hotel Statler, Washington, D. C. Scientific and clinical sessions will be given the days of Sept. 7, 8, 9, 10 and 11. All sessions will be open to members of the medical profession in good standing with the American Medical Association. In addition to the scientific sessions, the annual instruction courses will be held Sept. 7, 8, 9 and 10. These courses will be offered in two groups. One set of ten lectures will be based primarily on physics and physiology and attendance will be limited to physicians. One set of ten lectures will be more general in character and will be open to physicians as well as to physical therapists. The physical therapists must be registered with the American Registry of Physical Therapy Technicians. Full information may be obtained by writing to the American Congress of Physical Medicine, 30 North Michigan Avenue, Chicago 2, Illinois.

#### NAVAL HOSPITAL RESIDENCIES

Rear Admiral Clifford A. Swanson, MC, USN, Surgeon General and Chief of the Bureau of Medicine and Surgery, announces that a new residency in General Practice will be inaugurated in Naval Hospitals on July 1, 1948. The Professional Division of the Bureau of Medicine and Surgery has developed a residency in that phase of medicine which is required to augment the several medical specialties recognized by the American Specialty Boards in order to supplement the residency training program, now operative, which is designed toward specialization. The program, as planned, will cover a period of three years. During each year of this residency Medical Officers will receive six months of training in General Medicine and related specialties, and six months in General Surgery and related specialties. Instruction will be provided by the staffs of the hospitals and outstanding civilian visiting staffs. With the introduction of this type of training Navy medicine has recognized the great need of the General Practitioner in the field of medicine.

#### MEETING OF L. S. U. MEDICAL ALUMNI

The New Orleans District of the L. S. U. Medical Alumni Association will meet at a banquet at

Arnaud's Restaurant on June 10, at 7:30 p. m. Dr. Harold Stoke, President of Louisiana State University will be the principal speaker. Alumni should send \$3.50 for their reservations to the Secretary-Treasurer, L. S. U. Medical Alumni Association, L. S. U. Medical School, 1542 Tulane Avenue.

#### WOMAN'S AUXILIARY

The Woman's Auxiliary to the Louisiana State Medical Society held its annual meeting in conjunction with the 68th annual conference of the Louisiana State Medical Society April 12-14 in Monroe, La. Headquarters for the Auxiliary were in the Virginia Hotel.

Following registration on Monday a luncheon for all state officers and officers of the Ouachita Parish Auxiliary was given at the La Casa Tearoom. A pre-convention Executive Board Meeting was held following the luncheon with Mrs. James W. Warren presiding. Reports of chairmen were read.

The home of Dr. and Mrs. DeWitt Milam was the lovely setting for a tea Monday afternoon, when the members of the Ouachita Auxiliary honored the following: Mrs. Eustace Allen, President of the Woman's Auxiliary to the American Medical Association, Mrs. Olin S. Cofer, President, Woman's Auxiliary to the Southern Medical Association, Mrs. A. A. Herold, Treasurer, Woman's Auxiliary to the American Medical Association, Mrs. O. B. Owens, President-elect of the Woman's Auxiliary to the Louisiana State Medical Society, and Mrs. James W. Warren, President of the Woman's Auxiliary to the Louisiana State Medical Society.

Tuesday, the General Session of the Auxiliary was held in the Crystal Ball Room of the Virginia Hotel with the President, Mrs. James W. Warren of New Orleans presiding. The invocation was given by Msgr. J. C. Marsh, St. Matthews Catholic Church. The address of welcome was given by Mrs. J. E. Walsworth, President of the Ouachita Parish Auxiliary and the response by Mrs. T. E. Strain, President, Caddo Parish Auxiliary. Memorial Services were read by Mrs. A. Dent Tisdale and the benediction, a vocal solo, "The Lord's Prayer" by Mrs. A. M. Serex.

Greetings were given to the assembly from Dr. Gilbert Anderson, New Orleans, President 1947-48 of the State Society, Dr. Marion Hargrove, Shreveport, President-elect 1948-49, Dr. John G. Snelling, Monroe, Chairman of Convention, and Dr. A. V. Friedrichs, Chairman of Council on Medical Service and Public Relations. This Council has offered their facilities for printing and mailing a Quarterly Publication for the Auxiliary.

Mrs. Eustace A. Allen, President of the Woman's Auxiliary to the American Medical Association, brought greetings from National. Their aim is to double the membership of the Auxiliary. There are 130,000 doctors who belong to the A. M.



A. and only 35,000 wives to the Auxiliary. She complimented Louisiana and the South on their progressive attitude towards a broad Public Relations program and she further stated that we as individuals should study the Bulletin, Hygeia, AMA and State Journals and know our subject matter in order to aid our husbands in the "art of letting the public know what they are doing for their good."

Mrs. Olin S. Cofer, President of the Woman's Auxiliary to the Southern Medical Association, was introduced as an honored guest and brought us a splendid message from "Southern." The business meeting was adjourned until the afternoon. The doctors and their wives were entertained at a barbecue arranged by Dr. D. W. Milam and his Committee. At the afternoon session reports were given by the State Officers and Parish Presidents. A report on the A. M. A. convention was read from Mrs. George Taquino. Mrs. Arthur A. Herold gave a report on the Southern Medical Association Convention. Mrs. M. C. Wiginton gave a report as our representative to the Louisiana Rural Health Council.

After the transaction of old and new business election of officers was held followed by their introduction and installation by Mrs. H. B. Gessner. The incoming President announced that the Post-Convention and School of Instruction to be held Wednesday morning would be open to all delegates and guests.

A complimentary dinner-dance was held Tuesday evening on the Roof of the Virginia Hotel. Wednesday a luncheon and style show followed the meeting which climaxed three days of pleasure for members of the Auxiliary in attendance at the State Convention. Members of the Ouachita Parish Auxiliary distinguished themselves as "perfect hostesses" throughout the Convention. The following who served on special committees should especially be complimented: Mrs. DeWitt Milam, General Chairman; Mrs. J. E. Walsworth, President and Vice-Chairman; Chairmen of Committees: Mrs. Clifford U. Johnson, Registration; Mrs. C. P. Gray, Jr., Badge and Ticket; Mrs. Morgan Simonton, Supplies; Mrs. A. Dent Tisdale, Program; Mrs. P. L. Perot, Information; Mrs. J. W. Cummins, Transportation; Mrs. C. B. Flinn, Publicity; Mrs. A. Scott Hamilton, Luncheon; Mrs. H. V. Collins, Decorations; Mrs. Irving Wolff, Tea.

Mrs. F. U. Darby,  
Press and Publicity Chairman of  
The Woman's Auxiliary to the  
La. State Medical Society.

Following is the President's Annual Report for 1947-48.

As President of the Woman's Auxiliary to the Louisiana State Medical Society, I beg leave to submit the following report:

The Louisiana Auxiliary brings greetings and a warm welcome to our National President, Mrs. Eustace Allen; to our Southern President, Mrs. Olin Cofer; to our National Treasurer, Mrs. Arthur Herold, who are our honored guests. The Auxiliary feels that Louisiana has made a distinct contribution to the National Association this year in supplying a treasurer so capable as our own Mrs. Herold. We know her. We admire her for her ability and love her for herself. We are proud to have her represent us among the outstanding women on the National Board.

The term program as applied to our Auxiliary has come to encompass practically every phase of Auxiliary work, and has gone so far beyond the old idea of entertainment that it requires not only the program chairman to administer it, but the aid of the vice-presidents, councilors, committee chairmen and parish presidents. Remembering that we are liaison officers between doctors and the public, as Mrs. Allen has so well put it, we have acquired a desire to be better informed. So the program, per se, has taken on a more serious form in most Auxiliaries. Some of the many fine program topics that have been offered follow: Community Recreation; Medical Legislation in the 80th Congress; Social Problems of To-day; Status of Tuberculosis Control in Louisiana; Juvenile Delinquency; Early Diagnosis of Cancer, Trends in Nutrition.

Blood and Plasma Banks are sponsored by two Auxiliaries. Nearly every group reports work or donations to Red Cross, March of Dimes, and T. B. Seals. Wives of Lafourche doctors helped their husbands in the examination of pre-school children and 4H clubs. Such activities demonstrate a general awareness of social needs and community welfare.

In promoting the most vital project on our agenda, The Extension of Medical Services through Louisiana Physicians' Service, the Public Relations chairman has been of inestimable help, as well as in other phases of the general program. Radio programs, sponsored by Parish Medical Societies are being put on with the help of Auxiliaries. Monroe and Shreveport have active speakers bureaus, and when called on, send speakers to any organized club to talk on Voluntary Prepayment plans. Caddo, Rapides and East Baton Rouge had open meetings, well attended by the laity, at which facts about Louisiana Physicians' Service were presented. Guests were also told of the stupendous sums—\$118,000,000 in 1947—that the Federal government, through various agencies, has expended on propaganda for compulsory health insurance.

We have become keenly conscious of the need for improved health and medical service in rural areas, and our group has an active representative on the Louisiana Rural Health Council.

Louisiana has sponsored two new projects this

year. The first, Preservation of Medical Cultural Items, is designed to collect and preserve historical medical data. The State's medical history is especially rich, but unfortunately too many early records and documents have been lost in Louisiana, and an effort is now being made to save what is left. We are indebted to Mr. William D. Postell, Librarian of the State University Medical School, for stimulating an interest in this work by his enlightening addresses, delivered to a number of Auxiliaries.

Calcasieu has compiled a history of the early doctors of the parish; they have had good publicity on the subject with an editorial and a front page article in the local paper. A window display featured on Doctors' Day showed scrap books, pictures of old instruments, pictures of an early drug store. East Baton Rouge featured a history of doctors of the parish from 1880 to 1926. Shreveport had editorials and a full page of pictures of items of interest. A member of the Jefferson Davis group has compiled a history of the early doctors of the parish, and books and instruments are to be turned over to them soon.

The Second District has books, one published in 1834, a Fitch Scale, scientific papers. Iberville has obtained old scales, books, a cautery set, a baby resuscitator, pictures of older doctors and a copy of the minutes of the first meeting of the Parish Medical Society. Rapides, Ouachita and Orleans have appointed chairmen—the latter has a few instruments—and five parishes have had addresses on the subject. The outlook is encouraging.

While we have had no chairman for Student Nurse Recruitment, the second new project, a number of parishes and the Second District have been active. They are sponsoring talks to high school classes, having essays written, displaying posters and aiding local hospitals in their efforts to obtain students. Mrs. Donaldson of Second District, secured pledges from eleven girls to study nursing. We recognize the crucial need for nurses in both rural and urban areas and it behooves us to spend more effort to attract them.

A definite consciousness of the need to stress cancer control is shown in every parish report received. Activities include making dressings, having lectures, sponsoring essays, gifts of money, work in the April drive, presentation of films and radio programs, not only to Auxiliaries but to schools, parent-teacher groups and women's clubs. Members in many parishes serve as commanders, deputies, and campaign chairmen.

Doctors' wives in every parish have honored their husbands on their Day—March 30th. Some in the traditional manner, with parties; others by featuring exhibits of medical cultural items; some with donations to the Commemoration Fund. Gifts to this fund, for aid to needy widows of doctors, have totaled \$221.04, the largest for any one year

so far, bringing the total amount in the bank to \$780.79.

Our desire to have better informed members who are more conversant with topics of special interest to us as wives of doctors, is gratified by the report of the Bulletin Chairman. She reports that subscriptions have increased from 23 last September to 82 at the present time, a gain of 59. It is sincerely hoped that interest in the Bulletin may continue. I believe that it is not a mistake to say that programs in all lines of our work may be directly due to this wider use of the publication.

The chairman of Press and Publicity has each month supplied the State Journal with interesting material for the Auxiliary section. She has kept readers informed concerning the program and the accomplishments of the parish groups. The files of last year have been placed in the Archives. The historian has compiled an attractive book, not, however, without some difficulty. Some parishes have neglected to send her any material at all, and others have not sent as much as they should. Please keep this in mind another year and remember that the historian needs your help in order to keep a full record of Auxiliary accomplishments.

Several parishes have done outstanding work in securing subscriptions to Hygeia, notably Ouachita, home of the Chairman, where eighty subscriptions were obtained. Tangipahoa has an excellent record, with every member a subscriber, and Iberville has placed subscriptions in every school. Jefferson Davis, with only eleven members, has five readers of Hygeia, four of the Bulletin, nine each of the New Orleans and A. M. A. Journals. They, surely, are among our best informed members.

With the President of the United States, in a recent speech, openly favoring compulsory medical insurance, the State Medical Society supporting certain parts of the Taft Health Bill, and Congress reconvening in January, a definite impetus was given to interest in legislation. The chairman has supplied parishes with material from News Letters, A. M. A. Journals, pamphlets and other sources. A few groups, though not enough, have devoted programs to legislation.

There was no need for revision of by-laws this year, but your chairman has stood by, ready to be called on.

Two distinct time-saving services were rendered officers and members when the printing chairman had names and addresses of parish presidents placed on the stationery, and the year-book chairman included the addresses of all members in the larger towns and cities in the year-book.

Progress has been made in organization, with Vernon Parish, with eight members, joining our ranks. Washington, with fifteen members, has organized and elected officers. A four-parish group, with Ruston as the center, came into being in November, but shortly afterwards, due to illness of the leader, became inactive. Lafayette has again



become active, and we have the definite promise that St. Landry will again join us in the fall. It has been especially inspiring to see the large numbers of fine young women who have become members in all sections of the State. This argues well for the future of the Auxiliary. There is a total of 786 full paid members, 18 associate and 10 honorary, making a grand total of 812.

At the suggestion of the President-elect, Mrs. Owens, a committee was appointed at the February Board meeting to look into the matter of having an Auxiliary Publication. As a result, the State Council on Medical Services have offered their facilities for printing and mailing a Quarterly publication for the Auxiliary. This will be invaluable in bringing direct to the doctor's wife information she should have, increasing thereby the effectiveness of the Auxiliary program.

Our National officers have been a source of in-

spiration and encouragement throughout the year. The executive secretary, Miss Wolfe has been helpful and co-operative. My own Board and the membership as a whole have given me such support as few presidents even hope for. To all of you I am deeply grateful for a happy, albeit strenuous year.

May I also express sincere appreciation to the President and Executive Secretary of the Louisiana State Medical Society, Dr. Anderson and Dr. Talbot, and to Miss Shoemaker, their assistant; and to the members of the Advisory Board, Dr. Shirley Lyons, Dr. Charles Barker, and Dr. Rhodes Spedale, for their unfailing courtesy and assistance in solving Auxiliary problems.

Respectfully submitted,

Barbara P. Warren, President,  
Woman's Auxiliary to the Louisiana  
State Medical Society.

## BOOK REVIEWS

*Practical Office Gynecology:* By Karl John Karnaky, M. D. Springfield, Charles C. Thomas, 1947. Pp. 261. Price, \$7.50.

One is immediately impressed by the personal nature of this book and the varied indications advocated for stilbestrol. Nausea is encountered in 87 per cent of 3223 patients receiving stilbestrol but this disappeared in 94 per cent after four or five days of treatment.

The author prescribes stilbestrol for the various menstrual dysfunctions, threatened abortion, pre-operatively in control of hemorrhage, uterine bleeding in the presence of myomas, chronic salpingitis, et cetera.

It is repeatedly emphasized that where malignancy is suspected, a thorough curettage and examination for cancer is essential.

Karnaky deserves due credit for his enthusiastic and persistent use of stilbestrol, for he has been bold where others fear to tread. Much of the experimentation needs substantiating, as stilbestrol is no panacea.

The compilation of this office reference book is excellent and one will find a treatment definitely outlined for almost every gynecologic ailment. Dr. Louis Spivak contributes a short chapter on some psychological aspects of gynecology.

EUGENE H. COUNTISS, M. D.

*Ocular Therapeutics:* By Wm. J. Harrison, Ph.D., M. D., F. A. C. S., Springfield, Charles C. Thomas, publisher, 1947. Pp. 112. Price, \$3.50.

This pocket manual of approximately one hundred pages briefly presents a description of the properties, action and uses of the more frequent

drugs employed in ophthalmology. The use of moist heat and cold, buffer and isotonic solutions, and local anaesthetics are also briefly discussed in a very readable and understandable manner. Metric prescriptions accompany most of the drugs mentioned. Younger ophthalmologists and those who are employed in ophthalmic clinics and offices will find much of value in this small volume on which the publisher has also done an excellent job.

CHAS. A. BAHN, M. D.

*Gifford's Ocular Therapeutics, 4th. Edition:* By D. Vail, Philadelphia, Lea & Febiger, 1947. Pp. 336. Price, \$5.00.

Dr. Vail has rendered a needed service in revising this well known work. The current usages of miotics, antibiotics, vascular therapy, as well as thermo and electro therapy are discussed at some length. On the whole, the changes which have been made were well chosen and the literature thoroughly reviewed. Books on therapeutics are especially difficult to present understandingly. They are written on the assumption that the remedies suggested will be employed in patients whose ocular symptoms and disease have been completely and accurately diagnosed. Unfortunately, this is often not correct. In subsequent editions the author should consider greater coordination of local and bodily therapy. Rarer and less remedial ocular conditions are occasionally discussed at greater length than their practical importance apparently justifies in a work of this size. The basic principles involved in the care of frequent ophthalmic conditions such as the allergic or/and psychoso-

matic factors in ophthalmic diseases, as well as seborrheic blepharoconjunctivitis, should be explained at greater length for greater practicality. Especially for younger ophthalmologists and those not familiar with current literature, this volume is a must.

CHAS. A. BAHN, M. D.

*Osteotomy of the Long Bones:* By Henry Milch, M. D. Springfield, Charles C. Thomas, 1947. Pp. 294. Price, \$6.75.

*Osteotomy of the Long Bones* by Henry Milch is a readable, well organized, and short book. It appears to be designed to impart to the specialist or the serious student an understanding of the fundamental principles underlying osteotomies. It is not intended to show the novice how to do them.

Dr. Milch develops, step by step, one's understanding of the problems involved in osteotomies; from the maintenance of parallelism of the articular ends in the simple angular osteotomy, to the more complex relationships in multiple planes, which are involved in osteotomies about the hip. For that reason, this is a book to be read through and savored, rather than one to be skipped about in.

There are many practical and worth while features in this book that deserve commendation, among them are: the clear and complete discussion of treatment of inequalities of limb length, the detection and correction of torsional deformities, and the methods of obtaining either increased stability or increased range of motion in the pathological hip.

ARTHUR MAXWELL, M. D.

#### PUBLICATIONS RECEIVED

Blakiston Company, Philadelphia: *Human Physiology* (3rd edit.), by F. R. Winton, M. D., D. Sc. and L. E. Bayliss, Ph. D.

Lea & Febiger, Philadelphia: *Laboratory Diagnosis of Protozoan Diseases* (2nd edit.), by Charles Franklin Craig, M. D., M. A. (Hon.), D. Sc. (Hon.), F. A. C. S., F. A. C. P.

Medical Society of the County of Westchester, White Plains, New York: *History of the Medical Society of the County of Westchester 1797-1947.*

C. V. Mosby Company, St. Louis: *Neuroanatomy* (2nd edit.), by Fred A. Mettler, A. M., M. D., Ph. D.; *Synopsis of Pediatrics*, by John Zahorsky, A. B., M. D., F. A. C. P.

Charles C. Thomas, Springfield, Illinois: *Coronary Heart Disease*, by A. Carlton Ernestene, M. D.; *The Hospital Care of Neurosurgical Patients* (2nd edit.), by Wallace B. Hamby, M. D., F. A. C. S.

Williams and Wilkins Company, Baltimore: *The Biological Standardisation of the Vitamins* (2nd edit.), by Katharine H. Coward, D. Sc.; *Psychiatric Examinations of the School Child* by Muriel Barton Hall, M. D.; *Text-Book of Public Health* (12th edit.), by W. M. Frazer, O. B. E., M. D., Ch. B., M. Sc., D. P. H. and C. O. Stallybrass, M. D., Ch. B., D. P. H., M. R. C. S., L. R. C. P.

World Press, Inc., Denver: *War, Politics, and Insanity*, by C. S. Bluemel, M. A., M. D., F. A. C. P., M. R. C. S. (Eng.).













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